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## AMERICAN JOURNAL OF
# DISEASES of CHILDREN



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**AUGUST 1952**
**VOLUME 84 NUMBER 2**

Published Monthly by
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Jan. 4, 1911, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00



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THE A. M. A. AMERICAN JOURNAL OF DISEASES OF CHILDREN is published by the American Medical Association as a medium for the advancement of knowledge of the diseases of children and for the publication of scientific investigation in this field.

Communications regarding subscriptions, reprints, etc., should be addressed, A. M. A. AMERICAN JOURNAL OF DISEASES OF CHILDREN, American Medical Association, 535 North Dearborn Street, Chicago 10.

Manuscripts for publication, books for review and correspondence relating to contributions should be sent to Dr. Clifford G. Grulee, Chief Editor, Box 672, Evanston, Ill., or to any other member of the Editorial Board.

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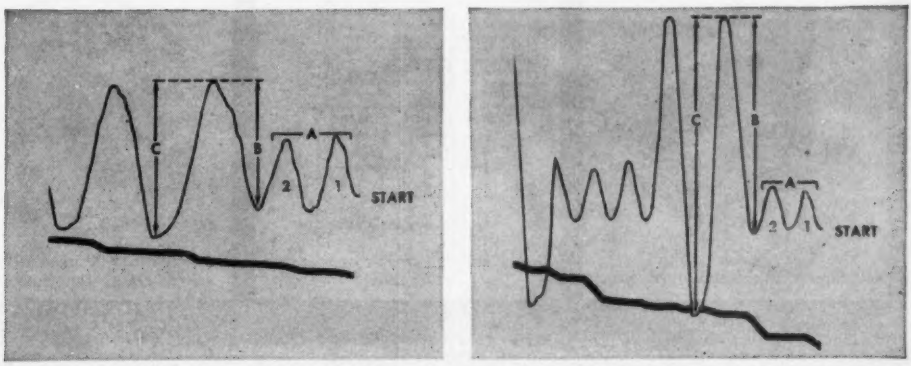


*A. Tidal breathing* *B. Complemental air* *C. Vital capacity*

Typical spirogram of asthmatic. Note marked diminution in vital capacity and complemental air; also, the over-all lengthening of the interval between inspiration and expiration.

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Schwartz, E., *J.A.M.A.* **147**: 1734–1737. Dec. 29, 1951.

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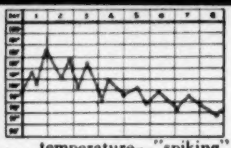
# URINARY TRACT

## *Pyelonephritis*

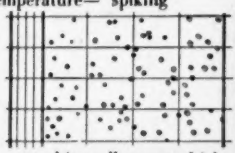
Pyelonephritis occurs most often in the young child . . .

commonest in the "diaper-age" female

The onset is sudden, usually with a chill . . .



. . . temperature—"spiking"



. . . white cell count—high

Always, pus cells and bacteria appear in the urine

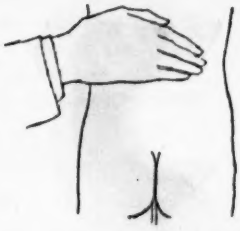
look for *clumps* of white cells in *catheterized* specimens

Culture determines pathogen. Mixed infection not uncommon.

in 8 out of 10 children, colon bacillus invades

Sometimes there is tenderness over the kidney region . . .

try the McKnight punch, or

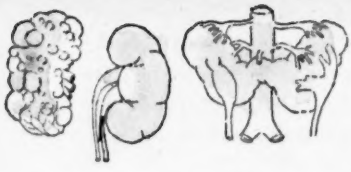


palpation in C-V angle

. . . or abdominal pain and rigidity

suggestive of an acute abdomen

Look for a cause of urinary stasis.



in children, 75% have congenital malformation . . . others may have calculus, foreign body, neoplasm, ureteral spasm.

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Many urinary tract infections
as well as other infections
rapidly respond to therapy
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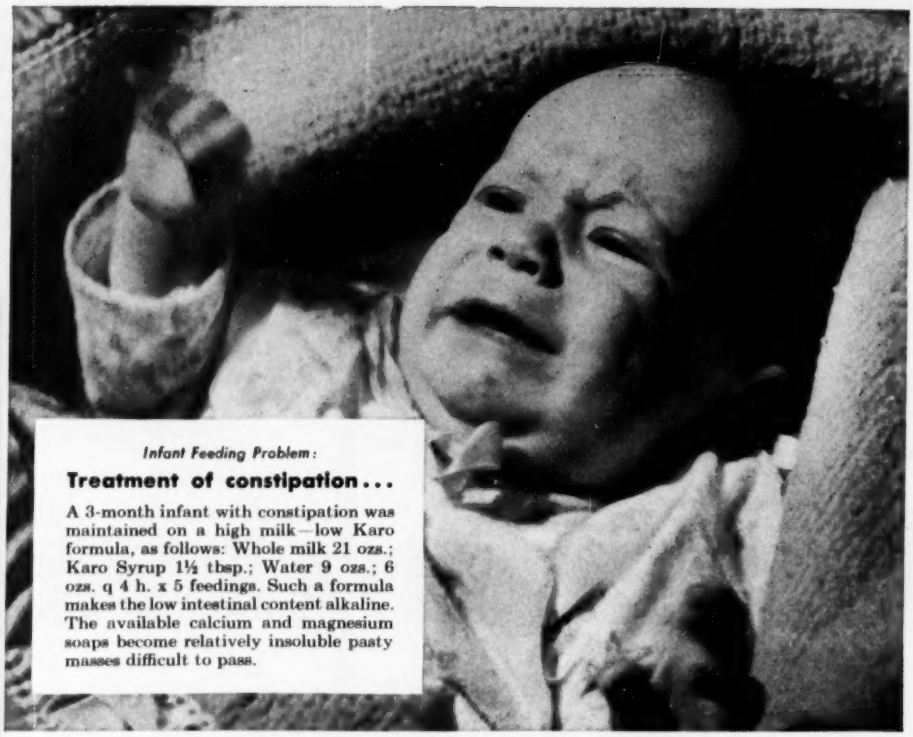

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A 3-month infant with constipation was maintained on a high milk—low Karo formula, as follows: Whole milk 21 ozs.; Karo Syrup 1½ tbsp.; Water 9 ozs.; 6 ozs. q 4 h. x 5 feedings. Such a formula makes the low intestinal content alkaline. The available calcium and magnesium soaps become relatively insoluble pasty masses difficult to pass.

**Recommendation:** Constipation was relieved by increasing the amount of Karo in the formula. A balance between the amount of milk and Karo is important in regulating the frequency and consistency of the stools.

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**Karo Syrup, 3 tablespoons** } **6 ozs. q 4 h. x 5 feedings**
**Water, 9 ozs.**

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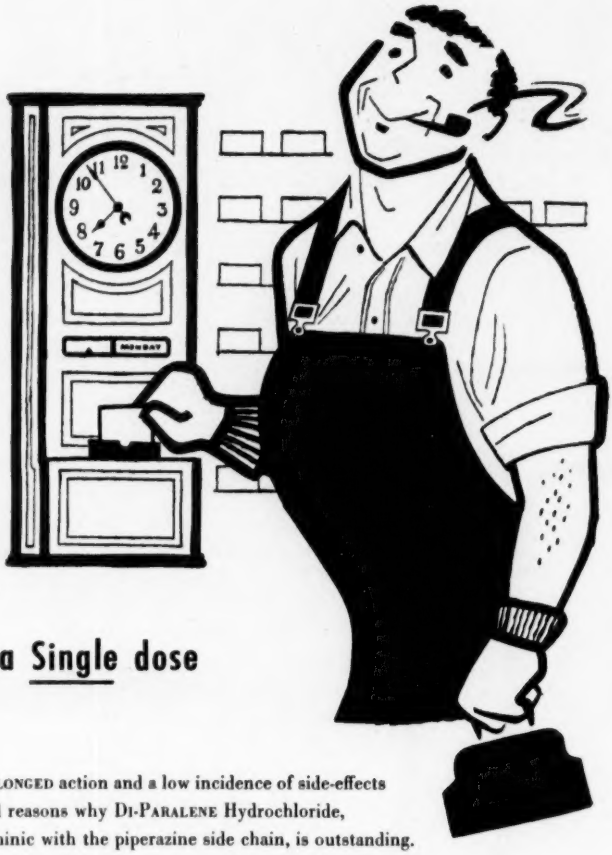

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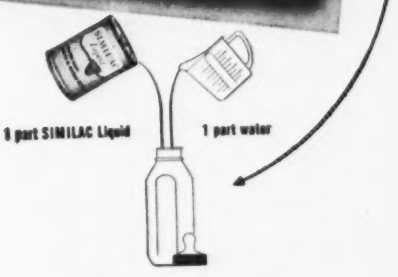


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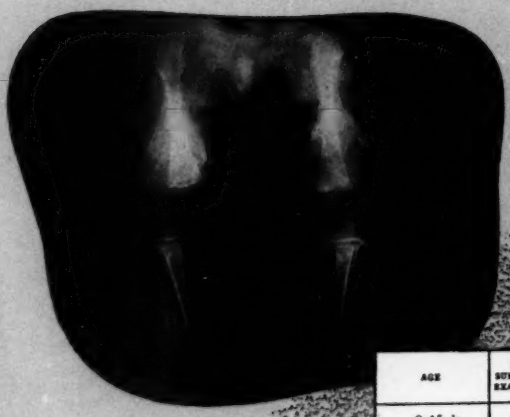
# SCURVY

## is more common



| AGE | NO. SUBJECTS EXAMINED | NO. WITH SCURVY | % WITH SCURVY | NO. WHITE SUBJECTS | NO. WITH SCURVY | NO. NEGRO SUBJECTS | NO. WITH SCURVY |
|---|---|---|---|---|---|---|---|
| 0–15 da. | 360 | 0 | 0 | 174 | 0 | 186 | 0 |
| 16–30 da. | 90 | 1 | — | 41 | 1 | 49 | 0 |
| 1 mo. | 99 | 0 | 0 | 48 | 0 | 51 | 0 |
| 2 mo. | 90 | 2 | 2.2 | 34 | 2 | 56 | 0 |
| 3 mo. | 69 | 3 | 4.3 | 31 | 3 | 38 | 0 |
| 4 mo. | 79 | 2 | 2.5 | 26 | 1 | 53 | 1 |
| 5 mo. | 73 | 12 | 16.5 | 25 | 3 | 48 | 9 |
| 6 mo. | 53 | 13 | 24.5 | 19 | 5 | 34 | 8 |
| 7 mo. | 54 | 10 | 18.5 | 22 | 7 | 32 | 3 |
| 8 mo. | 40 | 5 | 12.5 | 18 | 2 | 22 | 3 |
| 9 mo. | 38 | 10 | 26.3 | 12 | 4 | 26 | 6 |
| 10 mo. | 41 | 5 | 12.2 | 16 | 0 | 25 | 5 |
| 11 mo. | 40 | 3 | 7.5 | 12 | 0 | 28 | 3 |
| 12–23 mo. | 177 | 3 | — | 68 | 1 | 109 | 2 |
| Total..... | 1303 | 69 | | 546 | 29 | 757 | 40 |

PREVALENCE OF SCURVY

➤ ➤ ➤

## than many think

Histological examination* of bone structure in 1300 infant post mortems revealed that scurvy occurred more than 10 times as frequently as is usually shown by clinical diagnosis. The most susceptible age is from the fifth through the eleventh month, with approximately 17% of infants exhibiting the histological signs. Over half of the children with scurvy had never received supplemental vitamin C. How easy to prevent, when Florida citrus is so rich in vitamin C content — so convenient, so economical, and so pleasant to take!

** Bull. Johns Hopkins Hosp. 87:569, 1950.*

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A. M. A.
American Journal of Diseases of Children

VOLUME 84 AUGUST 1952 NUMBER 2

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# CORTICOTROPIN (ACTH) THERAPY OF INITIAL ATTACKS OF ACUTE RHEUMATIC FEVER IN CHILDREN

VINCENT C. KELLEY, M.D., Ph.D.
SALT LAKE CITY

THE INITIAL reports of Hench, Kendall, and co-workers [1] on the effects of hormonal preparations on rheumatoid arthritis and rheumatic fever furnished the impetus which has resulted in widespread intensive investigations on the efficacy of cortisone and corticotropin (ACTH) in the treatment of rheumatic fever.[2]

From the Department of Pediatrics of the University of Utah.

1. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Effect of Hormone of Adrenal Cortex (17-Hydroxydehydrocorticosterone: Compound E) and of Pituitary Adrenocorticotrophic Hormone on Rheumatoid Arthritis, Proc. Staff Meet., Mayo Clin. **24**:181, 1949. Hench, P. S.; Slocumb, C. H.; Barnes, A. R.; Smith, H. L.; Polley, H. F., and Kendall, E. C.: Effects of Adrenal Cortical Hormone 17-Hydroxy-Dehydrocorticosterone (Compound E) on Acute Phase of Rheumatic Fever, ibid. **24**:277, 1949.

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*(Footnote continued on next page)*

Results reported by various investigators have been widely divergent. Some of the more obvious factors contributing to the divergence of opinion concerning the response of rheumatic fever to these drugs are (1) the variability of the disease with regard to severity and duration of each of its protean manifestations, (2) variations in the criteria employed in establishing the diagnosis of rheumatic fever, (3) variations in dosage schedules of the drugs employed, (4) selection of cases in certain series to include primarily persons exhibiting predominantly some selected manifestation of rheumatic fever, and (5) failure to clearly differentiate among patients suffering from initial acute attacks, recurrent acute attacks, and a chronically active phase of rheumatic fever.

The purpose of this communication is to report the results of treatment with corticotropin of 18 consecutive unselected children with initial attacks of acute rheumatic fever. In the interests of clarity, no patients with recurrent or chronically active rheumatic fever, no patients treated with cortisone, and none of the 28 patients previous reported upon [2] are included.

## MATERIALS AND METHODS

The subjects in this study were 18 children, ranging in age from 3½ to 15 years, who were suffering with initial, acute attacks of rheumatic fever. Included were 11 boys and 7 girls. Therapy of each patient was initiated at the earliest possible moment after an unequivocal diagnosis could be established, in an attempt to determine, if possible, the effects of early treatment upon the manifestations of the acute disease and upon the extent of residual cardiac involvement.

The criteria employed in establishing the diagnosis of rheumatic fever were those as set forth by Denny, Wannamaker, Brink, Rammelkamp, and Custer,[4] which constitute a slight modification of those of Jones.[5] For a diagnosis of definite acute rheumatic fever, these criteria demand two major or one major and two minor manifestations of the disease. In the series of cases presented here, every patient had definite acute rheumatic fever according to these criteria; actually every patient exhibited at least two major manifestations of the disease.

All patients were maintained with bed rest but otherwise with standard hospital routine during the period of the study. Vital signs were recorded four times a day. The patients were given standard hospital diets with no restriction of sodium intake or other modification. No supplementary potassium was given. Most of the patients were treated daily with penicillin prophylactically, since facilities were not available for the application of adequate isolation techniques.

No salicylates or medications reputed to be of value in therapy of rheumatic fever, other than corticotropin, were administered. All patients receiving corticotropin therapy received ascorbic acid in a daily dose of 500 mg. However, it should be observed that the doses of ascorbic acid administered here are not of the same magnitude as those suggested by Massell and his

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Stachlin, D., and Wilson, D. L.: Medical Progress: The Clinical Usefulness of ACTH and Cortisone, ibid. **242**:783, 824 and 865, 1950. (*p*) Wilson, M. G., and Helper, H. N.: Effect of Pituitary Adrenocorticotropic Hormone (ACTH) in Acute Rheumatic Carditis, J. A. M. A. **145**:133, 1951.

3. Adams, F. H.; Kelley, V. C.; Dwan, P. F., and Glick, D.: Response of the Serum Hyaluronidase Inhibitor and Mucoproteins to Adrenocorticotropic Hormone in Rheumatic States. Mucolytic Enzyme Systems XV. Pediatrics **7**:472, 1951; in Mote, J. R.: Proceedings of the Second Clinical ACTH Conference, Vol. 2, Therapeutics, New York, The Blakiston Company, 1951, p. 572.

4. Denny, F. W.; Wannamaker, L. W.; Brink, W. R.; Rammelkamp, C. H., and Custer, E. A.: Prevention of Rheumatic Fever: Treatment of the Preceding Streptococcic Infection, J. A. M. A. **143**:151, 1950.

5. Jones, T. D.: The Diagnosis of Rheumatic Fever, J. A. M. A. **126**:481, 1944.

associates [6] for therapy in rheumatic fever. This ancillary medication was given as a precautionary measure in an attempt to eliminate one of the potential variables involved in the response of patients to corticotropin therapy. Both theoretical and practical justification for this measure exists. On a theoretical basis there is reason to expect the adequacy of ascorbic acid supply to the adrenal gland to influence adrenal response to corticotropin stimulation.[7] That this consideration is of practical significance is indicated by the observation previously reported [8] that certain patients who fail to respond to a given dose of corticotropin exhibit a dramatic response to the same dose after supplementation of therapy by daily administration of ascorbic acid.

In most cases the corticotropin was administered intramuscularly, the total daily dose being given in four equal portions at six-hour intervals. Therapy was initiated with a daily dose varying from 25 to 100 I. U., this initial dose being continued until the serum mucoprotein level had exhibited a substantial decrease toward normal [8] and, in certain cases, until the erythrocyte sedimentation rate had been less than 20 mm. per hour for several (three to five) days. Then the daily dose was tapered gradually according to the following plan. If the initial dose was greater than 40 I. U. per day, it was diminished by decrements of 20 I. U. until it had reached a level of 40 I. U. per day; below this dosage level the successive decrements in dose were each 10 I. U. until this resulted in discontinuance of the drug. Each successive decrement in dose of the drug was ordered only after a minimum time of two days at the previous dosage level and only if no evidence, clinical or chemical,[9] of recurrence of rheumatic activity had occurred.

In certain instances, after a trial of therapy with a particular daily dose of corticotropin (instituted empirically), the dose was increased on the assumption that the initial dose chosen had not been adequate. This decision was based on the failure of the erythrocyte sedimentation rate to begin to decrease within a period of seven to nine days, since with adequate daily dosage such decrease was uniformly observed within this period of time.[8] Without exception, in the present series of cases as well as in previous experiences, when the daily dose was increased a prompt and satisfactory response of the erythrocyte sedimentation rate resulted.

In a few cases corticotropin was administered by slow intravenous infusion, 25 I. U. of corticotropin in 500 cc. of 5% dextrose in water being given over a period of 12 hours during each day. The criteria and schedule employed in tapering the dose were the same as described above for intramuscular administration of corticotropin, except that the dose was diminished in decrements of 5 I. U. until this resulted in discontinuance of the drug.

These patients were subjected to frequent clinical and laboratory evaluation. Blood specimens were obtained by venipuncture approximately three times a week for determination of erythrocyte sedimentation rates and serum levels of various acute-phase reactants, including mucoproteins which were determined by a slight modification of the method of Winzler and his associates.[10] All patients were submitted to cardiac fluoroscopy and roentgenologic examination before initiation of therapy and at frequent intervals until the heart appeared normal upon such examination. Unipolar-lead electrocardiograms were taken before therapy and at approximately weekly intervals after initiation of therapy in all patients.

At the time of discharge from the hospital all of these patients were ambulatory and had only minor activity restriction. At the present time all of them who are of school age are attending school regularly.

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6. Massell, B. F.; Warren, J. E.; Patterson, P. R., and Lehuers, H. J.: Antirheumatic Activity of Ascorbic Acid in Large Doses: Preliminary Observations on 7 Patients with Rheumatic Fever, New England J. Med. **242**:614, 1950.

7. Sayers, G., and Sayers, M. A.: Pituitary-Adrenal System, Ann. New York Acad. Sc. **50**:522, 1949.

8. Adams and others.[8] Kelley, V. C.; Good, R. A., and McQuarrie, I.: Serum Mucoproteins in Children in Health and Disease, with Special Reference to Rheumatic Fever, Pediatrics **5**:824, 1950.

9. Several different acute-phase reactants were determined serially on the blood of all these patients; the results of these studies will be reported in detail elsewhere. However, for practical purposes, "chemical evidence of recurrence" as used here may be interpreted as meaning an elevation of the erythrocyte sedimentation rate.

10. Winzler, R. J.; Devor, A. W.; Mehl, J. W., and Smythe, I. M.: Studies on Mucoproteins of Human Plasma: I. Determination and Isolation, J. Clin. Invest. **27**:609, 1948.

OBSERVATIONS

Table 1 shows the distribution of major and minor rheumatic manifestations exhibited by these patients. Every patient in this series had definite carditis according to the criteria employed [4] and had objective and subjective evidence of arthritis, fever, and elevated erythrocyte sedimentation rate. In addition, most of these patients had one or more other major or minor manifestations of rheumatic fever.

*Case Summaries.*[11]—PATIENT 1.—T. L., a 7-year-old white boy, had been ill for four days before initiation of corticotropin therapy. The manifestations were carditis (cardiac enlargement, early right heart failure, an abnormal electrocardiogram with prolonged P-R interval, a grade 2 M.S. murmur, and tachycardia), severe polyarthritis, subcutaneous nodules, fever, arthralgia, and an elevated erythrocyte sedimentation rate. The dosage of corticotropin was 100 I. U. a day intramuscularly for 12 days, then tapered, and discontinued after 32 days, a total dose of 1,860 I. U. The arthritis was much improved 12 hours after initiation of therapy, and all evidence

TABLE 1.—*Manifestations of Rheumatic Fever Encountered in Eighteen Children with Initial Acute Attacks of the Disease*

| | No. of Cases |
|---|---|
| **Major manifestations** | |
| 1. Carditis | 18 |
| (*a*) Cardiac enlargement | 3 |
| (*b*) New murmur | 18 |
| (*c*) Friction rub | 3 |
| (*d*) Abnormal ECG | 14 |
| (*e*) Cardiac failure | 1 |
| 2. Migratory polyarthritis | 18 |
| 3. History of recurrence | 0 |
| 4. Chorea | 3 |
| 5. Subcutaneous nodules | 2 |
| **Minor manifestations** | |
| 1. Fever | 18 |
| 2. Abdominal pain | 3 |
| 3. Arthralgia | 18 |
| 4. Erythema marginatum | 3 |
| 5. Erythema multiforme | 1 |
| 6. Epistaxis | 4 |
| 7. Elevated erythrocyte sedimentation rate* | 18 |

* Wintrobe method.

of arthritis and arthralgia had disappeared two days after initiation of therapy. There was no evidence of laboratory or clinical rebound after discontinuation of therapy. This patient was seen only once after discharge from the hospital, approximately one month after discharge, and at that time had no murmur or evidence of cardiac involvement of any type.

PATIENT 2.—J. N., a 5-year-old white girl, had been ill for 16 days before institution of corticotropin therapy. The manifestations were carditis (grade 2 M.S. and grade 3 M.D. murmurs, friction rub, an abnormal electrocardiogram, and tachycardia), severe polyarthritis, fever, arthralgia, and elevated erythrocyte sedimentation rate. Polyarthritis was of such severity that she was unable to move either leg, and for this reason she came to this hospital with a referral diagnosis of poliomyelitis. The initial dose of corticotropin was 100 I. U. intramuscularly daily for nine days. The dose then was tapered and the drug discontinued after 46 days. The total dose was 2,210 I. U. Within 24 hours after initiation of this therapy, the child was able to move her legs freely with only moderate discomfort, and after 48 hours all evidence of arthritis and arthralgia had disappeared. After discontinuance of therapy she exhibited no clinical evidence but moderate laboratory evidence of rebound, with the erythrocyte sedimentation rate becoming

11. Intensities of cardiac murmurs are designated according to Levine's classification (Levine, S. A.: The Systolic Murmur, J. A. M. A. **101**:436, 1933), and the localization in time and position are designated as follows: M, mitral; A, aortic; S, systolic; D, diastolic.

elevated to 29 mm. per hour and requiring nine days to return to normal. She was last seen one month after discharge from the hospital, at which time she had a grade 1 M.S. murmur which was audible only with the patient in a supine position.

PATIENT 3.—P. S., a 6-year-old white boy, had been ill for 12 days before the institution of corticotropin therapy. The manifestations were carditis (grade 2 M.S. and grade 1 M.D. murmurs, tachycardia), mild polyarthritis, arthralgia, fever, abdominal pain, epistaxis, and elevated erythrocyte sedimentation rate. The dosage was 40 I. U. intramuscularly for 21 days, then tapered, and discontinued after 30 days. The total dose was 1,020 I. U. There was no clinical or laboratory evidence of rebound. This patient was last seen four months after discharge from the hospital, at which time he had a grade 1 M.S. murmur and no other evidence of rheumatic fever.

PATIENT 4.—M. F., a 9-year-old white boy, had been ill for 14 days before initiation of corticotropin therapy. The manifestations were carditis (cardiac enlargement, grade 3 M.S. and grade 1 M.D. murmurs, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), migratory polyarthritis, chorea, fever, arthralgia, and elevated erythrocyte sedimentation rate. The initial dose was 40 I. U. per day intramuscularly. The initial clinical response was good, but laboratory evidence of rheumatic activity persisted. For this reason, after 22 days of therapy the daily dose of corticotropin was increased to 60 I. U. The total duration of therapy before tapering of the dose was 47 days and before discontinuance was 63 days. The total dose was 2,590 I. U. This patient was most uncooperative and refused consistently to stay within prescribed activity limits. The patient was last seen seven months after discharge from the hospital, at which time he had no murmurs or other evidence of rheumatic residua.

PATIENT 5.—J. B., a 14-year-old white girl, had been ill for 11 days prior to institution of corticotropin therapy. The manifestations were carditis (grade 2 M.S. murmur, friction rub, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), migratory polyarthritis, fever, arthralgia, erythema multiforme, and elevated erythrocyte sedimentation rate. The dosage was 40 I. U. intramuscularly for 12 days, then tapered, and discontinued after 36 days. The total dose was 920 I. U. There was no evidence of rebound, laboratory or clinical, after discontinuation of therapy. The patient was last seen 10 months after discharge from the hospital, at which time she had no murmurs and no evidence of rheumatic residua.

PATIENT 6.—T. F., a 6-year-old white boy, had been ill for nine days before institution of corticotropin therapy. The manifestations were carditis (grade 2 M.S. murmur, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), migratory polyarthritis, chorea, fever, arthralgia, erythema marginatum, and elevated erythrocyte sedimentation rate. The dosage was 40 I. U. intramuscularly per day for 17 days, then tapered, and discontinued after a total of 26 days. The total dose was 890 I. U. After discontinuation of therapy he exhibited no clinical or laboratory evidence of rebound. This patient was last seen eight months after discharge from the hospital, at which time he had a grade 1 M.S. murmur and no other rheumatic residua.

PATIENT 7.—L. L., a 7-year-old white boy, had been ill for four days before institution of corticotropin therapy. The manifestations were carditis (grade 2 M.S. and grade 1 M.D. murmurs, friction rub, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), severe migratory polyarthritis, fever, abdominal pain, arthralgia, and elevated erythrocyte sedimentation rate. The dosage was 60 I. U. intramuscularly per day for 13 days, then tapered, and discontinued after 33 days. The total dose was 1,210 I. U. Upon institution of corticotropin therapy the polyarthritis was markedly improved in one day, and all evidence of arthritis and arthralgia had disappeared in two days. On the 21st day of therapy the temperature became elevated; the murmurs and friction rub, which had disappeared, reappeared; the P-R interval again became prolonged, and the erythrocyte sedimentation rate, which had been normal, increased to 38 mm. per hour. There was an eosinophilia of 8% at this time. The dose had at this time been reduced to 20 I. U. per day, and this flare-up is interpreted as meaning that the dose had been reduced too rapidly. The dose was not increased but was maintained at this level for 17 days, and at the end of this time all evidence of the recrudescence of activity had disappeared. The dose then was tapered and discontinued with no further evidence of rebound. This patient was last seen one month after discharge from the hospital, and at that time had no murmur and no evidence of rheumatic residua.

PATIENT 8.—W. W., a 10-year-old Negro boy, had been ill for 11 days before initiation of corticotropin therapy. The manifestations were carditis (grade 2 M.S. murmur, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), migratory polyarthritis, fever, arthralgia, and elevated erythrocyte sedimentation rate. He was treated with 25 I. U. of corticotropin intravenously for one day but refused to tolerate this method of administration, On the 2d day of therapy the dose was changed to 25 I. U. per day intramuscularly and on the 15th day to 60 I. U. per day intramuscularly because of failure to respond to the previous dose. This dose was continued through the 30th day, then tapered, and discontinued after the 38th day. The total dose was 1,515 I. U. Following the withdrawal of therapy there was no clinical or laboratory evidence of rebound. The patient was last seen four months after discharge from the hospital and at that time had no murmur or other rheumatic residua.

PATIENT 9.—H. B., a 9-year-old white girl, had been ill for 19 days before initiation of corticotropin therapy. The manifestations were carditis (grade 2 M.S. and grade 1 M.D. murmurs, cardiac enlargement, and tachycardia), migratory polyarthritis, chorea, fever, arthralgia, epistaxis, and an elevated erythrocyte sedimentation rate. An initial daily dose of 40 I. U. of corticotropin was given intramuscularly. Because of failure of the patient to respond adequately, this dose was increased to 60 I. U. per day on the 25th day of therapy, continued at this level through the 46th day, and then gradually tapered. With decreasing doses she exhibited a rebound to the extent of a labile pulse and an elevation of the erythrocyte sedimentation rate to 25 mm. per hour. For this reason, the dose was tapered only very gradually and was finally discontinued on the 85th day. The total dose was 3,390 I. U. After discontinuance of therapy no laboratory or clinical rebound occurred. She was last seen seven months after discharge from the hospital and at that time had a soft grade 1 M.S. murmur and no evidence of rheumatic activity.

PATIENT 10.—S. C., a 14-year-old white girl, had been ill for three days before initiation of therapy. The manifestations were carditis (grade 2 M.S. murmur and an abnormal electrocardiogram with prolonged P-R interval), migratory polyarthritis, fever, arthralgia, and elevated erythrocyte sedimentation rate. The dosage was 100 I. U. a day intramuscularly for 9 days, then gradually tapered, and finally discontinued after 52 days. The total dose was 2,480 I. U. This girl exhibited an excellent initial response to corticotropin, but, as the dose was reduced, a moderate laboratory rebound (interpreted as resulting from too rapid tapering of dose) occurred with reelevation of the P-R interval to the upper limits of normal and of the erythrocyte sedimentation rate to 26 mm. per hour. A slight elevation of the erythrocyte sedimentation rate persisted for 47 days. However, therapy was discontinued late during this period, with no obvious deleterious effect and no clinical or laboratory evidence of rebound. She was last seen six months after discharge from the hospital and had at that time no murmur or other rheumatic residua.

PATIENT 11.—R. M., a 15-year-old Mexican boy, had been ill for 12 days before initiation of therapy. The manifestations were carditis (grade 1 M.S. murmur, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), severe migratory polyarthritis, fever, arthralgia, and an elevated erythrocyte sedimentation rate. The dosage was 100 I. U. per day intramuscularly for 33 days, then tapered, and discontinued after 63 days. The total dose was 4,720 I. U. The polyarthritis improved remarkably in one day and disappeared completely in two days. The erythrocyte sedimentation rate increased moderately as the dose was decreased, but, since there was no clinical evidence of rebound, the tapering of dose was continued cautiously and use of the drug was finally discontinued while the erythrocyte sedimentation rate remained slightly elevated. No evidence of reactivation of the rebound occurred when the drug was withdrawn, and the patient went on to uneventful recovery. The maximum erythrocyte sedimentation rate observed during the rebound was 49 mm. per hour, and the total elapsed time from the first evidence of rebound until the rate was again normal was 66 days. The patient was last seen three months after discharge from the hospital and at that time had no murmurs or other evidence of rheumatic fever.

PATIENT 12.—K. I., a 14-year-old white boy, had been ill for five days before initiation of corticotropin therapy. The manifestations were carditis (grade 2 M.S. murmur and tachycardia), moderate migratory polyarthritis, fever, arthralgia, and an elevated erythrocyte sedimentation rate. The dosage was 100 I. U. per day intramuscularly for 33 days, then tapered, and discontinued after 64 days. The total dose was 4,790 I. U. This patient was most uncooperative and

consistently refused to stay within activity restrictions, a fact which in his case was felt to contribute to his relatively poor response. As the dose was tapered, there was laboratory evidence but no clinical evidence of rebound. At this time the erythrocyte sedimentation rate increased to 47 mm. per hour and returned only very slowly to normal, requiring 78 days to come within normal limits. In the meantime the corticotropin had been withdrawn without apparent effect upon the course of this rebound. The patient was last seen five months after discharge from the hospital and at that time had no murmur or evidence of rheumatic fever.

PATIENT 13.—S. S., an 8-year-old white girl, had been ill for 10 days before institution of corticotropin therapy. The manifestations were carditis (grade 2 M.S. murmur, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), severe migratory polyarthritis, fever, arthralgia, and an elevated erythrocyte sedimentation rate. Therapy was initiated with 40 I. U. per day intramuscularly. This dose was increased to 100 I. U. per day on the 11th day, when it became apparent that the initial dose was inadequate; it was maintained at this level through the 33d day, then gradually tapered, and finally discontinued after 115 days of therapy. The total dose was 6,170 I. U. Withdrawal of corticotropin resulted in laboratory but no clinical rebound, with the erythrocyte sedimentation rate becoming elevated to 42 mm. per hour and requiring 40 days to return to normal limits. The patient was last seen five months after discharge from the hospital and at that time had no murmur or other evidence of rheumatic fever.

PATIENT 14.—L. C., a 3½-year-old white girl, had been ill for five days before initiation of corticotropin therapy. The manifestations were carditis (grade 1 M.S. murmur and tachycardia), moderately severe arthritis, fever, arthralgia, and an elevated erythrocyte sedimentation rate. The dosage was 40 I. U. per day intramuscularly for 12 days, then tapered, and discontinued after 36 days. The total dose was 1,040 I. U. On the 18th day of therapy an upper respiratory infection developed which resulted in laboratory but no clinical evidence of rebound. The dosage of corticotropin, which had been partially tapered, was increased again to 40 I. U. per day and then gradually retapered. The child was last seen 11 months after discharge from the hospital, at which time she had no murmur or other evidence of rheumatic residua.

PATIENT 15.—A. I., a 12-year-old white boy, had been ill for 42 days before initiation of corticotropin therapy. The manifestations were carditis (grade 2 M.S. murmur, friction rub, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), migratory polyarthritis, subcutaneous nodules, fever, arthralgia, erythema marginatum, epistaxis, and an elevated erythrocyte sedimentation rate. He had been partially treated with inadequate doses of cortisone for a short time before admission. Upon admission he was immediately treated with a daily dose of 40 I. U. of corticotropin intramuscularly, which was continued for 16 days, then tapered, and discontinued after the 20th day. The total dose was 700 I. U. He showed no clinical or laboratory evidence of rebound after discontinuation of therapy. He was last seen four months after discharge from the hospital, at which time only a barely audible M.S. murmur was heard.

PATIENT 16.—K. H., an 8-year-old white girl, had been ill for five days previous to institution of corticotropin therapy. The manifestations were carditis (grade 2 M.S. murmur, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), severe migratory polyarthritis, fever, abdominal pain, arthralgia, erythema marginatum, and an elevated erythrocyte sedimentation rate. The dosage was 25 I. U. per day intravenously for 17 days, then tapered, and discontinued after the 19th day. The total dose was 450 I. U. After discontinuation of therapy she exhibited no clinical or laboratory evidence of rebound. The patient was last seen seven months after discharge from the hospital. At that time there was no murmur or other evidence of rheumatic fever.

PATIENT 17.—M. M., a 9-year-old white boy, had been ill for two days before initiation of corticotropin therapy. The manifestations were carditis (grade 2 M.S. and grade 1 A.D. murmurs, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), severe migratory polyarthritis, fever, and an elevated erythrocyte sedimentation rate. The polyarthritis was so severe in this boy that he was unable to move either lower extremity, and on this basis he had entered the hospital with a referral diagnosis of poliomyelitis. The dosage of corticotropin was 25 I. U. per day intravenously for 23 days, then tapered, and discontinued after the 33d day. The total dose was 720 I. U. Within 24 hours after institution of therapy the boy could move his legs freely with only minimal pain, and within two days all evidence of arthritis and arthralgia

had disappeared. After withdrawal of therapy there was no clinical or laboratory evidence of rebound. The patient was last seen five months after discharge from the hospital, at which time no murmurs or other rheumatic residua were observed.

PATIENT 18.—A. D., an 11-year-old Indian boy, had been ill five days before initiation of corticotropin therapy. The manifestations were carditis (grade 3 M.S. murmur, an abnormal electrocardiogram with prolonged P-R interval, and tachycardia), severe migratory polyarthritis, fever, arthralgia, and an elevated erythrocyte sedimentation rate. He was admitted to the hospital with a referral diagnosis of poliomyelitis, based on his inability to move either leg because of the severity of the polyarthritis. The dosage of corticotropin was 25 I. U. per day intravenously for 14 days, then tapered, and discontinued after a total of 20 days. The total dose was 305 I. U. He had responded dramatically to this therapy, with the arthritis and arthralgia improving markedly within 12 hours and disappearing completely within 2 days, the temperature becoming normal in 12 hours, the electrocardiogram returning to normal limits in 6 days, and the erythrocyte sedimentation rate returning to normal in 10 days. However, within three days after discontinuance of therapy his symptoms had begun to recur, and within five days he was more critically and severely ill than he had been upon his admission to the hospital. At this time, in addition to all the evidences of rheumatic activity previously enumerated, he had cardiac enlargement and definite evidence of early right heart failure. Corticotropin therapy was then reinstituted with 100 I. U. per day intramuscularly for 13 days. The dose then was tapered and finally discontinued after 26 days. The total dose was 1,820 I. U. Within one day after reinitiation of therapy, the temperature returned to normal and the arthritis improved remarkably, subjectively and objectively. Within two days the arthritis and arthralgia had disappeared. Within eight days the erythrocyte sedimentation rate was normal and the evidence of cardiac failure had disappeared. The electrocardiogram remained abnormal for 18 days. The patient went on to clinical recovery and manifested no laboratory or clinical evidence of rebound after withdrawal of corticotropin. He was last seen 11 months after discharge from the hospital, and at that time no murmur was audible. By exercising the patient it was possible to cause a soft systolic apical murmur to appear briefly in a well-localized area.

*Summary of Corticotropin Therapy.*—In Table 2 are summarized the data on corticotropin therapy of these patients with their initial attacks of acute rheumatic fever. These children had been ill from 2 to 42 days before therapy was instituted. Fifteen were treated by intramuscular administration of corticotropin and three by intravenous administration of the drug. One patient, A. D., was treated first with corticotropin intravenously with an excellent response. However, when the treatment was discontinued the boy had a recurrence of symptoms and was re-treated with the drug intramuscularly.

The initial daily dose of corticotropin administered intramuscularly varied from 25 to 100 I. U. The maximum daily dose administered by this route to different patients ranged from 40 to 100 I. U. The total amount of corticotropin used per patient varied from 450 to 6,170 I. U., with the average total dose being 2,155 I. U. The total amount of corticotropin administered in terms of I. U. per pound (0.5 kg.) of body weight of the patient ranged from 8.6 to 89.4, with a mean value of 31.5 I. U. per pound. The total duration of treatment ranged from 19 to 115 days, with an average duration of 46½ days.

Analysis of the data of Table 2 indicates that initiation of corticotropin therapy with an inadequate daily dose [12] of the drug is an expensive error, both with regard to the cost of the drug and with regard to the cost of hospitalization. For those

12. As used here an "inadequate daily dose" is considered as one which does not bring about a definite decrease in the erythrocyte sedimentation rate within a period of seven to nine days after initiation of therapy, and an "adequate daily dose" as one which does bring about such a decrease.

patients whose initial daily doses were inadequate and required an increase after a trial therapy, the average total duration of treatment was 75 days, the average total amount of drug used was 3,418 I. U., and the average total International Units required per pound of body weight was 54.5. For those patients whose initial daily dose proved to be adequate, the corresponding values were, respectively, 40 days, 1,985 I. U., and 29.9 I. U. per pound. It may be observed that each of the latter values is only slightly greater than half the corresponding value for those patients whose therapy was initiated with an inadequate daily dose.

The problem of predicting on an empirical basis the most economical dose with which to initiate therapy in a given patient is a complex one, certain aspects of which are illustrated by analysis of the data of Table 2. For example, those patients

TABLE 2.—*Corticotropin Therapy of Patients with Initial Attacks of Acute Rheumatic Fever*

| Patient No. | Age, Yr. | Sex | Weight, Lb. | Duration Before Therapy, Days | Daily Dose: Initial I. U. | Daily Dose: Initial I. U./Lb. | Daily Dose: Maximum I. U. | Daily Dose: Maximum I. U./Lb. | Total Dose I. U. | Total Dose I. U./Lb. | Duration of Treatment, Days: Maximum Dosage | Duration of Treatment, Days: Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 7 | M | 48 | 4 | 100 | 2.1 | 100 | 2.1 | 1,860 | 38.7 | 12 | 32 |
| 2 | 5 | F | 46 | 16 | 100 | 2.2 | 100 | 2.3 | 2,210 | 47.2 | 9 | 46 |
| 3 | 6 | M | 41 | 12 | 40 | 1.0 | 40 | 1.0 | 1,020 | 24.9 | 21 | 30 |
| 4 | 9 | M | 57 | 14 | 40 | 0.7 | 60 | 1.1 | 2,500 | 45.4 | 47 | 63 |
| 5 | 14 | F | 107 | 11 | 40 | 0.4 | 40 | 0.4 | 920 | 8.6 | 12 | 36 |
| 6 | 6 | M | 38 | 9 | 40 | 1.1 | 40 | 1.1 | 890 | 23.4 | 17 | 26 |
| 7 | 7 | M | 56 | 4 | 60 | 1.1 | 60 | 1.1 | 1,210 | 21.6 | 18 | 33 |
| 8 | 10 | M | 75 | 11 | 25 | 0.3 | 60 | 0.8 | 1,515 | 20.2 | 30 | 38 |
| 9 | 9 | F | 54 | 19 | 40 | 0.7 | 60 | 1.1 | 3,390 | 62.8 | 46 | 85 |
| 10 | 14 | F | 100 | 3 | 100 | 1.0 | 100 | 1.0 | 2,480 | 24.8 | 9 | 52 |
| 11 | 15 | M | 138 | 12 | 100 | 0.7 | 100 | 0.7 | 4,720 | 34.2 | 33 | 63 |
| 12 | 14 | M | 78 | 5 | 100 | 1.3 | 100 | 1.3 | 4,790 | 61.4 | 33 | 64 |
| 13 | 8 | F | 69 | 10 | 40 | 0.6 | 100 | 1.4 | 6,170 | 89.4 | 31 | 115 |
| 14 | 3½ | F | 30 | 5 | 40 | 1.3 | 40 | 1.3 | 1,040 | 34.7 | 12 | 36 |
| 15 | 12 | M | 75 | 42 | 40 | 0.5 | 40 | 0.5 | 700 | 9.3 | 16 | 20 |
| 16 | 8 | F | 83 | 5 | 25 IV | 0.3 | 25 IV | 0.3 | 450 | 5.4 | 17 | 19 |
| 17 | 9 | M | 63 | 2 | 25 IV | 0.4 | 25 IV | 0.4 | 720 | 11.4 | 23 | 33 |
| 18 | 11 | M | 72 | 5 | 25 IV<br>100 IM | 0.3<br>1.4 | 25 IV<br>100 IM | 0.3<br>1.4 | 305<br>1,820 | 4.2<br>25.3 | 14<br>13 | 20<br>26 |
| Mean value for all patients whose therapy was initiated with..... | | | | | (*a*) An adequate daily dose | | | | 1,985 | 29.9 | .. | 40 |
| | | | | | (*b*) An inadequate daily dose | | | | 3,418 | 54.5 | .. | 75 |
| | | | | | (*c*) 100 I. U./day | | | | 2,980 | 38.6 | .. | 47 |
| | | | | | (*d*) 40 I. U./day | | | | 2,090 | 37.3 | .. | 51 |

who were initially given a dose of 100 I. U. per day required an average total dose of 2,980 I. U., as compared to the smaller average total dose of 2,090 I. U. required by those patients who were initially given a dose of 40 I. U. per day. However, in this series, on the average, those patients whose therapy was initiated with 100 I. U. per day were larger children than those whose therapy was initiated with 40 I. U. per day. When this is taken into account, it is seen that the two groups of patients required nearly identical amounts of corticotropin per pound of body weight, with those on the 100-I. U. schedule requiring a total of 38.6 I. U. per pound and those on the 40 I. U. schedule requiring a total of 37.3 I. U. per pound. The patients on the 100-I. U. schedule required a slightly shorter treatment period, 47 days as compared to 51 days for those patients on the 40-I. U. schedule. This would mitigate toward the use of the 100-I. U. schedule, since the total dose required in terms of I. U. per pound is practically identical on each schedule.

However, that the larger daily dosage schedule is wasteful of corticotropin and of hospitalization days in some cases is shown by comparing the data of the patients

on this schedule with those of all patients whose therapy was initiated with an adequate daily dose regardless of the size of this dose. In the latter group the average total amount of corticotropin required was only 1,985 I. U., as compared to 2,980 I. U. for those patients on the 100-I. U. schedule; the total International-Unit-per-pound requirement was only 29.9, as compared to 38.6 for those patients on the 100-I. U. schedule; and the total duration of treatment required was only 40 days, as compared to 47 days. Thus, employment of a standard initial daily dose of 100 I. U. would be wasteful, because it would constitute overdosage in many cases. On the other hand, the use of a 40-I. U. daily initial dose would be approximately equally wasteful of corticotropin and of hospital time, as indicated previously, because this would constitute underdosage in many cases.

The implication has been made repeatedly [2] that dosage of corticotropin cannot be based upon body weight but must be empirical. Analysis of the data of Table 2 yields reason to question this statement. If the patients whose data are presented here are divided into two groups, those whose initial dose was less than 1 I. U. per pound per day and those whose initial dose was greater than 1 I. U. per pound per day, it is apparent that the latter group exhibited a definitely more satisfactory response to therapy. They required, on the average, only 1,924 I. U. of corticotropin for total treatment as compared to 2,858 I. U., only 33.6 I. U. per pound as compared to 38.6 I. U. per pound, and, most important, only 38 $\frac{3}{10}$ treatment days as compared to 60 treatment days. On the basis of these data the conclusion is drawn that the initial daily dose of corticotropin should be between 1 and 2 I. U. per pound and that doses either too high or too low are wasteful of corticotropin and of hospital days.

The foregoing applies to intramuscular therapy with corticotropin. The data included here with regard to intravenous therapy are insufficient to warrant any conclusions. My personal experience with intravenous therapy has been limited to the three cases listed here and seven additional cases. Of the total of 10 patients, one refused to tolerate the prolonged periods of intravenous administration, one failed to respond satisfactorily even to three times the usual dose, and eight responded well initially to 25 I. U. per day. However, six of these eight had almost immediate recurrence of symptoms and signs of acute rheumatic fever when therapy was discontinued. Although intravenous therapy has the decided advantage over intramuscular therapy of requiring considerably smaller amounts of corticotropin, this advantage is probably more than offset in the treatment of children by the difficulties of administering the drug by this route.

*Clinical Response to Corticotropin Therapy.*—Table 3 summarizes the data with regard to the clinical response of this group of patients with initial attacks of acute rheumatic fever to corticotropin therapy. Joint symptomatology usually showed definite improvement within a few hours to one day and usually had disappeared completely within two days. The temperature was normal within one day in eight patients, within two days in five additional patients, and within five days in all patients. For all but two of these patients, the electrocardiogram had returned to normal within two weeks. In those patients treated with intramuscularly administered corticotropin in an initial dose which proved to be adequate and which did not have to be increased, the average time for the return of the sedimentation rate to normal limits was 13½ days.

TABLE 3.—*Response to Corticotropin Therapy of Patients with Their Initial Attack of Acute Rheumatic Fever*

| Patient No. | Duration of Symptoms Before Treatment, Days | Maximum Daily Dosage ACTH, I. U. | Joint Involvement at Initiation of Therapy | Joint Involvement | | Days Until Temperature Normal | Days Until ECG Normal | Initial E. S. R. | Days Until E. S. R. Normal |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Days Until Improved | Days Until Disappeared | | | | |
| 1 | 4 | 100 I. M. | Severe | ½ | 2 | 1 | 26 | 80 | 12 |
| 2 | 16 | 100 I. M. | Severe | 1 | 2 | 2 | 13 | 58 | 12 |
| 3 | 12 | 40 I. M. | 0 | .. | .. | 4 | 0 | 53 | 19 |
| 4 | 14 | 60 I. M. | Moderate | ½ | 1 | 1 | 3 | 57 | 41 |
| 5 | 11 | 40 I. M. | Moderate | 1 | 2 | 1 | 3 | 50 | 4 |
| 6 | 9 | 40 I. M. | 0 | .. | .. | 0 | 0 | 53 | 17 |
| 7 | 4 | 60 I. M. | Severe | 1 | 2 | 1 | 2 | 55 | 6 |
| 8 | 11 | 60 I. M. | 0 | .. | .. | 3 | 5 | 54 | 25 |
| 9 | 19 | 60 I. M. | 0 | .. | .. | 4 | 0 | 56 | 43 |
| 10 | 3 | 100 I. M. | Severe | 1 | 2 | 2 | 8 | 54 | 11 |
| 11 | 12 | 100 I. M. | Moderate | 1 | 2 | 2 | 0 | 56 | 26 |
| 12 | 5 | 100 I. M. | Moderate | ½ | 1 | 2 | 0 | 51 | 33 |
| 13 | 10 | 100 I. M. | Moderate | 1 | 2 | 3 | 11 | 52 | 38 |
| 14 | 5 | 40 I. M. | Moderate | ½ | 1 | 2 | 0 | 49 | 7 |
| 15 | 42 | 40 I. M. | 0 | .. | .. | 1 | 12 | 34 | 5 |
| 16 | 5 | 25 I. V. | Severe | 2 | 5 | 5 | 11 | 55 | 9 |
| 17 | 2 | 25 I. V. | Severe | ½ | 1 | 1 | 3 | 57 | 20 |
| 18 | 5 | 25 I. V. | Severe | ½ hr. | 2 | ½ | 6 | 54 | 10 |
| 18 | Rebound | 100 I. M. | Severe | 1 | 2 | 1 | 18 | 49 | 8 |

TABLE 4.—*Auscultatory Findings in Eighteen Patients with Initial Attacks of Acute Rheumatic Fever*

| Patient No. | Murmurs Recorded During Acute Phase of Attack* | Murmurs Recorded at Most Recent Examination | Length of Follow-Up Study, Mo. |
|---|---|---|---|
| 1 | 2 M. S. | 0 | 1 |
| 2 | 2 M. S.<br>3 M. D. | 1 M. S. | 1 |
| 3 | 2 M. S.<br>1 M. D. | 1 M. S. | 4 |
| 4 | 3 M. S.<br>1 M. D. | 0 | 7 |
| 5 | 2 M. S. | 0 | 10 |
| 6 | 2 M. S. | 1 M. S. | 8 |
| 7 | 2 M. S.<br>1 M. D. | 0 | 1 |
| 8 | 2 M. S. | 0 | 4 |
| 9 | 2 M. S.<br>1 M. D. | 1 M. S. | 7 |
| 10 | 2 M. S. | 0 | 6 |
| 11 | 1 M. S. | 0 | 3 |
| 12 | 2 M. S. | 0 | 5 |
| 13 | 2 M. S. | 0 | 5 |
| 14 | 1 M. S. | 0 | 11 |
| 15 | 2 M. S. | 1 M. S. | 4 |
| 16 | 2 M. S. | 0 | 7 |
| 17 | 2 M. S.<br>1 A. D. | 0 | 5 |
| 18 | 3 M. S. | 0 | 11 |

* The following abbreviations are used: M., mitral; A., aortic; S., systolic; D., diastolic. Numerals refer to intensity of murmur.[11]

*Follow-up Study of Patients.*—The follow-up study of the patients has been brief, ranging from 1 to 11 months. Approximately half these patients exhibited some laboratory evidence of the rebound phenomenon immediately after discontinuance of therapy. However, after final discontinuation of therapy none of these patients showed clinical evidence of rebound, and none of them have suffered recurrent attacks of acute rheumatic fever.

Although it is fully realized that the cardiac status of these patients will be subject to change and that therefore no meaningful conclusions with regard to the influence of corticotropin therapy on the cardiac damage produced by rheumatic fever can be drawn, certain observations regarding their present cardiac status are in order. Table 4 shows the auscultatory findings recorded at the height of the acute attack of rheumatic fever and at the most recent examination of each patient. It will be observed that 13 of these patients now have no residual murmur. Each of the remaining five patients has a grade 1 mitral systolic murmur, but in one case this murmur is barely or inconstantly audible. Of this group of patients six had significant diastolic murmurs during their acute illnesses, all of which have disappeared.

## COMMENT

There has been virtual unanimity of opinion among all investigators who have reported on the treatment of rheumatic fever with corticotropin or cortisone that there is a pronounced beneficial effect of these drugs on manifestations of the disease other than manifestations of carditis. Similarly, in the present study, there was observed a striking amelioration and shortening of the duration of such symptomatology. Especially with regard to the manifestations of arthritis and of fever, these patients responded definitely better than might have been anticipated with other modes of therapy. Likewise, the response of the sedimentation rate in those patients whose daily dose was considered adequate, according to the criteria employed, was dramatic.

The response of manifestations of carditis, other than cardiac mumurs, in these patients was heartening. Since discontinuation of therapy none of these patients has had evidence of cardiac enlargement, abnormal electrocardiogram, or other evidence of active carditis. This observation agrees with those of other investigators [13] who have observed a beneficial effect of hormone therapy on the manifestations of rheumatic carditis.

There is increasing evidence that the pathology of rheumatic fever consists of a diffuse involvement of tissues of mesenchymal origin.[14] An important constituent of such tissues is hyaluronic acid.[15] Inferential evidence that hyaluronic acid metabolism is disturbed in patients with rheumatic fever has arisen from the demonstrations of

13. Footnote *2e*, *i*, *j*, *k*, and *p*.

14. Rich, A. R., and Gregory, J. E.: Experimental Evidence that Lesions with the Basic Characteristics of Rheumatic Carditis Can Result from Anaphylactic Hypersensitivity, Bull. Johns Hopkins Hosp. **73**:239, 1943. Fox, R., and Jones, L.: Vascular Pathology in Rabbits Following Administration of Foreign Protein, Proc. Soc. Exper. Biol. & Med. **55**:294, 1944. Keefer, C. S.: Rheumatic Heart Disease: A Phase of Rheumatic Fever, Internat. Clin. **1**:116, 1942. Cohen, H.: The Metabolism of Hyaluronic Acid in Relation to Rheumatic Diseases, Ann. Rheumat. Dis. **8**:31, 1949.

15. Meyer, K.: The Biological Significance of Hyaluronic Acid and Hyaluronidase, Physiol. Rev. **27**:335, 1947.

elevation of serum-hexosamine levels,[16] polysaccharide levels,[17] mucoprotein levels,[8] and nonspecific hyaluronidase-inhibitor levels [18] during the acute phase of the disease and their return to normal with its quiescence, whether spontaneous or induced by administration of corticotropin. These observations suggest that the fundamental pathology of the disease may be influenced by the administration of corticotropin and that the duration of the persistence of the biochemical aberrations characteristic of the active phase of the disease may be shortened by corticotropin therapy.

The conclusion that hormone therapy of rheumatic fever is merely suppressive has been so frequently stated in the literature [19] that this has become a widely accepted principle of therapy. It should be recalled, however, that this conclusion has been based upon a limited number of cases and a very limited variety of therapeutic regimens. The observation previously reported [3] that clinical and laboratory rebound occurs commonly if corticotropin therapy is discontinued suddenly without tapering or before the serum-mucoprotein level has manifested a substantial decrease toward normal, and much less commonly if the drug dosage is carefully tapered, suggests that the therapeutic regimen must be highly individualized. The complete absence of clinical evidence and the low incidence of laboratory evidence of rebound after final discontinuation of therapy in the present series of patients corroborate and emphasize this observation. Perhaps final acceptance of the conclusion that hormone therapy of rheumatic fever is merely suppressive should be held in abeyance, pending the accumulation of further definitive evidence.

That over a prolonged period of observation the apparent extent of cardiac damage of a rheumatic fever patient may either increase or decrease remarkably is a well-established fact.[20] The valvular damage resultant from an attack of rheumatic fever may be considered to be due to late proliferative changes following subsidence of the inflammatory process which occurs during the acute phase of the disease or to a long-continuing low-grade inflammatory process. In either case, if a course of therapy with corticotropin actually terminates the patient's rheumatic activity, such therapy should be of benefit in decreasing the incidence and severity of residual cardiac damage, and the earlier this therapy is initiated the greater should be the

16. Kelley, V. C.: Acute Reactants: II. Serum Hexosamines in Patients with Rheumatic Fever and Related Diseases, J. Pediat. **40**:413, 1952.

17. Kelley, V. C.: Acute Phase Reactants: I. Serum Non-Glucosamine Polysaccharides in Patients with Rheumatic Fever and Related Conditions, J. Pediat. **40**:405, 1952.

18. Adams and others.[3] Good, R. A., and Glick, D.: Mucolytic Enzyme Systems: IX. Non-Specific Hyaluronidase Inhibitor in Rheumatic Fever, J. Infect. Dis. **86**:38, 1950. Dorfman, A., and Moses, F. E.: Effect of Adrenocorticotropic Hormone (ACTH) on Serum Hyaluronidase Inhibitor in Rheumatic Fever, Proc. Soc. Exper. Biol. & Med. **73**:667, 1950. Hakanson, E. Y., and Luft, R.: Effect of ACTH Protein and ACTH Polypeptide on Hyaluronidase Inhibitor of Human Serum, Acta endocrinol. **3**:318, 1949. Schmith, K., and Faber, V.: Fall in Hyaluronidase Inhibition in Serum During Administration of Adrenocorticotropic Hormone (ACTH), ibid. **3**:310, 1949.

19. Footnote 2*c*, *d*, *g*, *h*, and *l*.

20. Bland, E. F.; White, P. D., and Jones, T. D.: Development of Mitral Stenosis in Young People, with Discussion of Frequent Misinterpretation of Mid-Diastolic Murmur at Cardiac Apex, Am. Heart J. **10**:995, 1935. Bland, E. F.; Jones, T. D., and White, P. D.: Disappearance of Physical Signs of Rheumatic Heart Disease, J. A. M. A. **107**:569, 1936. Bland, E. F., and Jones, T. D.: Delayed Appearance of Heart Disease After Rheumatic Fever, ibid. **113**:1380, 1939. Bland, E. F., and Jones, T. D.: Rheumatic Fever and Rheumatic Heart Disease: A 20-Year Report on 1,000 Patients Followed Since Childhood, Circulation **4**:836, 1951.

benefit. On the other hand, if corticotropin therapy is merely suppressive and the patient can be expected to exhibit continuing rheumatic activity after cessation of therapy, a less beneficial effect upon the eventual cardiac status of the patients is to be anticipated.

Certain it is that the present series of observations is inadequate to answer the question of whether early initiation of corticotropin therapy in adequate daily dosage and continuation of such therapy for an adequate period of time will prevent or ameliorate the patient's eventual cardiac residual damage resultant from an attack of rheumatic fever. However, the encouragingly low incidence of evidence that residual cardiac damage is persisting in this small, briefly followed series of patients suggests that this approach to the problem should be more extensively pursued and evaluated.

The question concerning the nature and severity of side-effects from hormone therapy demands consideration. The adverse effects that have been observed in this series of patients have consisted of temporary production of moon-shaped facies, gain in weight, abnormal appetite, occurrence of reddish-purple striations over the buttocks and the thighs, appearance or aggravation of acne, and mild temporary glycosuria. In no case has it been necessary to discontinue therapy because of side-effects. These effects have all been temporary and have receded promptly upon discontinuation of therapy.

That certain severe complications may result from the use of corticotropin or cortisone in therapy cannot be denied. Whether the danger involved is imminent enough to constitute a serious contraindication to their employment in treatment is a question which cannot be answered categorically at this time. The final answer to this question will depend upon the eventual evaluation of the efficacy of this type of therapy as well as of the statistical risk of serious complications.

## SUMMARY

Eighteen children suffering with initial attacks of acute rheumatic fever were treated with corticotropin (ACTH) at the earliest possible time after establishment of an unequivocal diagnosis.

Symptoms of acute rheumatic fever of these patients responded dramatically to corticotropin therapy.

After a short period of follow-up study, 13 of these patients have no residual evidence of cardiac involvement and 5 have grade 1 mitral systolic murmurs.

On the basis of data presented, the conclusion is drawn that the optimal initial daily dose of corticotropin is between 1 and 2 I. U. per pound (0.5 kg.) of body weight.

This investigation was supported in part by a research grant from the National Institutes of Health, United States Public Health Service, Bethesda, Md. Support by the Utah Rheumatic Fever Association and of the Utah State Federation of Business and Professional Women's Clubs was also received.

Much of the corticotropin used in this study ("acthar") was supplied by The Armour Laboratories.

Mary C. O'Brien and Doris Kirschvink gave technical assistance.

# LACK OF EFFECT OF SUPPLEMENTARY VITAMIN $B_{12}$ ADMINISTERED TO PREMATURE INFANTS

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REPORTS of several investigators have indicated that vitamin $B_{12}$ has growth-promoting properties.[1] The possibility that this compound might be of especial benefit to premature infants, as an accelerator of growth and hematopoiesis, has been put to test by a number of clinics, with entirely negative results.[2]

The present study is concerned with 117 infants admitted to the premature nursery of Baltimore City Hospitals in 1950. Studies were made of the weight gain, the hemoglobin levels, and the red blood cell counts of two groups of premature infants; one group comprised infants who received a daily oral supplement of 30 $\mu$ of a solution of crystalline vitamin $B_{12}$, and the other was a control group.

## METHODS

Upon admission to the premature nursery infants were assigned alternately to the vitamin-$B_{12}$ group and to the control group. All infants received similar care during the first week of life. By this time all were established on feedings of a low-fat milk (alacta®) with 8% carbohydrate added. Beginning with the eighth day of life all infants were given a daily supplement of 0.6 cc. of an aqueous polyvitamin preparation ("polyvisol"). Those infants previously designated as the vitamin-$B_{12}$ group were given in addition a daily oral supplement of 30 $\mu$ of vitamin $B_{12}$. Data on infants who died and on two infants with severe congenital malformations are not included in the results.

Feedings were increased in small increments in conformation with the usual policy of the nursery, weight and appetite being used as criteria. Under this system, regardless of the calculated caloric requirement, feedings are advanced only when it is observed that the infant will accept a larger amount; should a voracious appetite be manifested, the calories ingested may reach or exceed 200 calories per kilogram per day. While this is not a truly ad lib. feeding program, there is considerable individual flexibility based on the infants' appetites. The responsible physician did not ordinarily know which infants were receiving the vitamin $B_{12}$ and which were the controls. Patients were weighed twice weekly until they reached the discharge weight of 2,410 gm. (5 lb., 5 oz.). A hemoglobin determination (Sahli's method) and a red blood cell count were done at the age of one week, biweekly thereafter, and upon discharge. In accordance with previously established policy, whenever the hemoglobin level fell below 9 gm. per 100 cc., the infant received a transfusion of fresh whole blood.

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1. (*a*) Wetzel, N. C.; Fargo, W. C.; Smith, I. H., and Helikson, J.: Growth Failure in School Children as Associated with Vitamin $B_{12}$ Deficiency: Response to Oral Therapy, Science **110**:651, 1949. (*b*) Chow, B. F.: Sequelae to the Administration of Vitamin $B_{12}$ to Humans, J. Nutrition **43**:323, 1951.

2. (*a*) Downing, D. F.: Failure of Vitamin $B_{12}$ to Promote Growth of Premature Infants, Science **112**:181, 1950. (*b*) Rascoff, H.; Danewitz, A. and Norton, R.: The Weight Progress of Premature Infants Given Supplementary Feedings of Vitamin $B_{12}$, J. Pediat. **39**:61, 1951. (*c*) Mitchell, T.; Etteldorf, J. N.; Tuttle, A. H., and Clayton, G. W.: Crystalline Vitamin $B_{12}$ and Sodium Folvate in Prematurity, Pediatrics **8**:821, 1951.

## RESULTS

Table 1 shows a comparison between 54 infants receiving vitamin $B_{12}$ and 63 control infants with respect to average birth weight, average hospital days required to reach the discharge weight of 2,410 gm., and the calculated average daily weight gain. Separate statistical analyses by sex were carried out because of the sex differences in growth response to vitamin $B_{12}$ found in animal experiments by other investigators.[3] These yielded no additional information. It is readily seen that there is a striking similarity between the two groups for the factors analyzed.

Table 2 presents a summary of the hematological data for the infants on whom the information was complete. The values at the time of attainment of discharge weight (2,410 gm.) are used, since this was invariably the lowest value for those patients who did not receive transfusions. In the case of the group given transfusions

TABLE 1.—*Comparative Data on Weight*

| | Infants, No. | Average Birth Weight, Gm. | Average Time to Reach 2,410 Gm., Days | Average Weight Gain per Day, Gm. |
|---|---|---|---|---|
| Controls | 63 | 1,740<br>Range = 878-2,293<br>S. D. = 331 | 36.7<br>Range = 18-93<br>S. D. = 15.6 | 18.2 |
| Vitamin $B_{12}$ group | 54 | 1,800<br>Range = 934-2,293<br>S. D. = 323 | 34.5<br>Range = 15-90<br>S. D. = 17.5 | 17.7 |

TABLE 2.—*Comparative Hematological Data*

| | Infants, No. | Hemoglobin, Average upon Discharge, Gm./100 Cc.* | R. B. C., Average upon Discharge, Millions * | Patients Transfused, No. |
|---|---|---|---|---|
| Controls | 60 | 12.5<br>S. D. = 2.68 | 3.7 | 10 |
| Vitamin $B_{12}$ group | 45 | 12.9<br>S. D. = 2.94 | 3.7 | 8 |

* When patients received transfusions, the value used was the one preceding the first transfusion.

the value used in computation of the average was the first determination falling under the 9-gm.-per-100-cc. lower limit set by the study protocol. This was deemed justifiable in view of the universal progressive fall in values mentioned above. It is again obvious that there is no significant difference between the two groups.

## COMMENT

The papers of Wetzel [1a] and Chow [1b] indicated a growth-promoting property of orally ingested vitamin $B_{12}$ in certain children. If the vitamin-$B_{12}$ content of the diet of the premature infant fed cow's-milk mixtures was less than optimum, its addition to the diet should produce increased growth. The striking hematopoietic activity of this substance in certain anemic states constituted another reason for assessing its activity in premature infants.

3. McCollum, E. B., and Chow, B. F.: Sex Differences in the Weight-Stimulating Effect of $B_{12}$ in Rats on Diets of Varying Composition, Proc. Soc. Exper. Biol. & Med. **75**:20, 1950.

Downing [2a] administered vitamin $B_{12}$ parenterally to a group of premature infants, without growth-promoting effect. Rascoff and his associates,[2b] using a small oral supplement of 5$\mu$, also noted no increase in weight gain as compared with a control group. Mitchell and his co-workers [2c] studied the effects of parenterally administered vitamin $B_{12}$ upon the weight and hematologic status of premature infants and found no benefits from its use. The present study, differing chiefly in that a relatively large oral dose was used, is confirmatory of the findings of these investigators. The data herein presented add statistical weight to the growing evidence that the addition of vitamin $B_{12}$ to that supplied by usual cow's milk feeding mixture does not increase the rate of growth nor prevent the usual fall of hemoglobin.

## CONCLUSION

Daily administration of an oral supplement of 30$\mu$ of vitamin $B_{12}$ produced no demonstrable effect upon premature infants with regard to growth or hematologic status. These data together with those of Mitchell [2c] and others indicate that there is no justification for the routine use of this substance in premature care.

# FOUR SIBLINGS WITH HEPATIC DISEASE LEADING TO CIRRHOSIS

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CIRRHOSIS of the liver has been frequently reported in children, and reference has often been made to multiple cases in families. However, the familial and genetic aspects of cirrhosis are not generally recognized. It is the purpose of this communication, first, to report the histories of four sisters all of whom were seen by one of us (L. F. R.) and who died within the first three months of life with postmortem findings of cirrhosis of the liver, and second, to evaluate briefly familial factors underlying cirrhosis of the liver in children.

## REPORT OF CASES

The parents of these children were of primarily Scandinavian extraction, unrelated by blood, and in good health. The mother's first pregnancy resulted in a boy infant who showed no abnormalities and is now living and well.

CASE 1.—As a result of the second pregnancy, which was normal, a full-term girl was born Jan. 4, 1934, with a birth weight of 3,950 gm. This baby seemed normal at the time of delivery, except for bilateral talipes varus. On the 10th day of life, vaginal bleeding was first noted; this was slight at birth but became more profuse by the 12th day, at which time 15 cc. of whole blood was administered intramuscularly from the mother. That day the child also had clonic convulsions lasting two hours, with a bulging fontanel and nuchal rigidity. This was thought to be due to a cerebral hemorrhage.

On the 14th day of life, the infant had hematemesis and epistaxis in treatment of which she again received 15 cc. of whole blood intramuscularly from her mother. On succeeding days she bled from the umbilical cord and from the site of injection of subcutaneous fluids. Because of this she was given more blood, both intramuscularly and intravenously, from her mother and other donors. Jaundice and clay-colored stools were first noted at this time. When she was 25 days old distention of the abdomen with dilatation of the superficial abdominal veins was first noted. This increased gradually until the patient's death on Feb. 10 at the age of 36 days. The clinical diagnosis was portal obstruction.

*Autopsy Findings.*—Examination revealed a grade 4 jaundice with marked distention of the abdomen. The peritoneal cavity was filled with bile-tinged fluid. The liver extended 2 cm. below the costal margin. All tissues appeared to be jaundiced and otherwise normal, except for the liver. It weighed 200 gm., cut with difficulty, and sounded "sandy" as it was cut. The gall bladder contained a thick mucoid dark bile. It was thought by the pathologist that there was some obstruction at the cystic duct. Microscopic sections of the liver showed an increase in the fibrous elements in the periportal spaces, with some inspissation of the bile. Fatty areas were present but were not very numerous, as seen in Figure 1*A*.

From the Department of Pediatrics and the Dight Institute of Human Genetics, University of Minnesota.

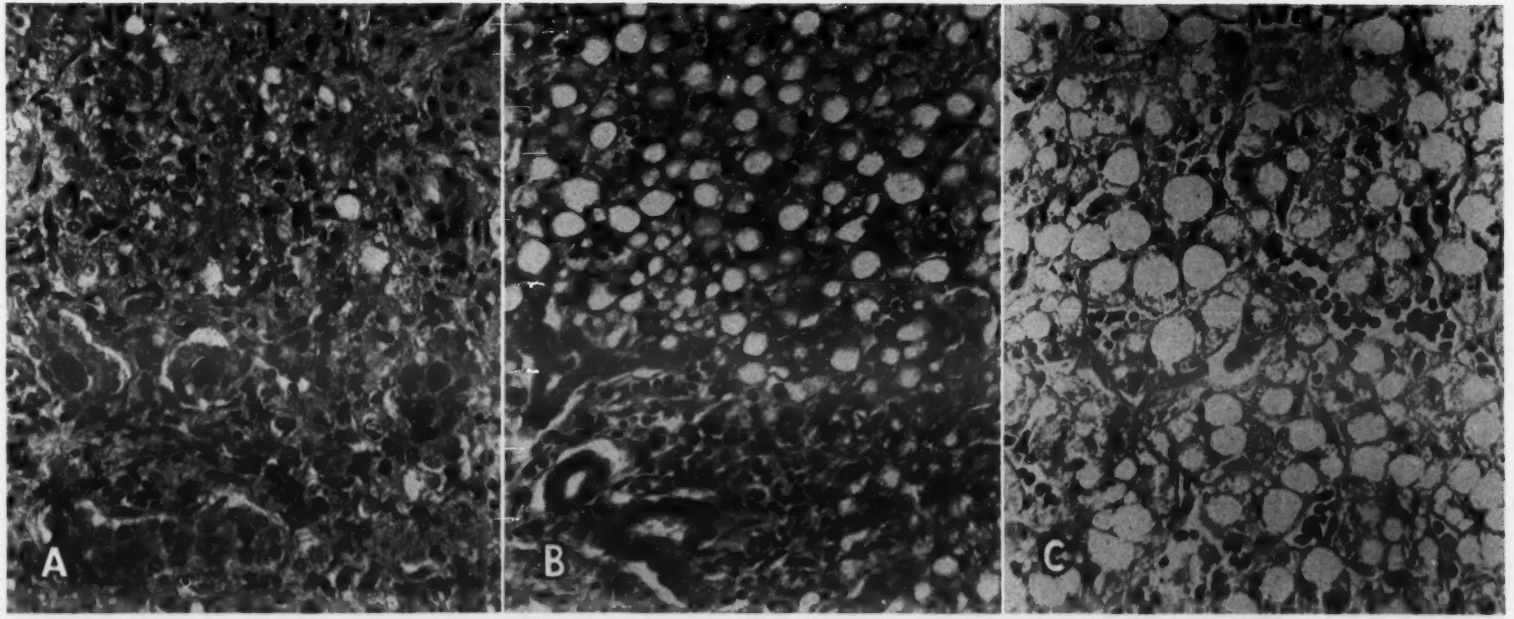


Fig. 1.—Photomicrographs of liver. *A* (Case 1), section closely resembles congenital atresia of the bile ducts except for the presence of fatty metamorphosis; bile thrombi and an increased number of bile ducts are easily seen; × 300. *B* (Case 2), showing presence of some liver cells and new bile-duct formation with accompanying high-grade fatty metamorphosis; × 300. *C* (Case 3), showing nearly complete absence of liver cells and high grade of fatty metamorphosis; × 300. No evidence of cirrhosis was present in the liver sections of this infant.

CASE 2.—The third pregnancy was normal, and a full-term girl was born Feb. 25, 1937, with a birth weight of 3,990 gm. This baby appeared normal at birth but was a poor eater at first, and for that reason she received parenteral fluids. On the sixth day of life, projectile vomiting developed, and physical examination revealed abdominal distention with some vaginal bleeding. The next day jaundice was first noted. Soon after this, her condition became more

Fig. 2 (Case 4).—Photograph of infant at the time of admission to the University Hospitals at the age of 11 days. Pencil mark across abdomen indicates the liver border.

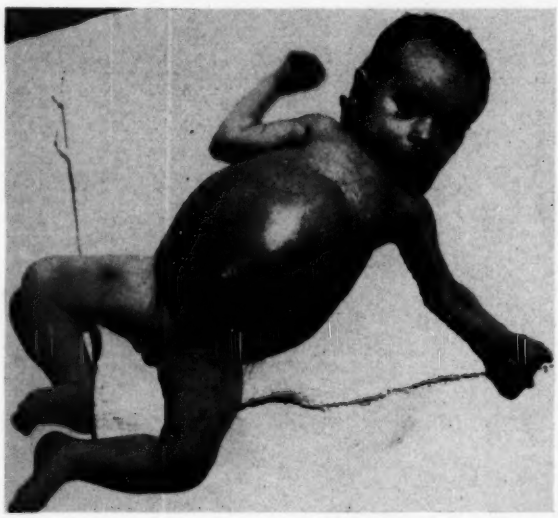

Fig. 3 (Case 4).—Photograph of infant at 1½ months of age. Note marked abdominal distention secondary to ascites, with evidence of developing collateral blood flow over the anterior abdominal wall.

critical with the development of severe abdominal distention and cyanosis. In spite of supportive therapy, including blood transfusion, she died on the 10th day of life.

*Autopsy Findings.*—Examination revealed moderate cyanosis of the body but only slight jaundice. There was congestion of the brain, spleen, and mesentery, and the organs were otherwise normal, with the exception of the liver. It weighed 220 gm. and had a smooth surface, but when sectioned it appeared to be fatty. Microscopic sections of the liver revealed

extensive fatty replacement in the parenchyma, with some mononuclear infiltration around the bile ducts, as seen in Figure 1*B*.

CASE 3.—The fourth pregnancy was normal, and a full-term girl was born Jan. 20, 1941. During the first five days of life there was no evidence of abnormality. On the sixth day the infant began to vomit and was found to have abdominal distention and jaundice. On the seventh day the liver was noted to be enlarged. This and the jaundice and vomiting increased progressively until the baby died on the 11th day of life. Small hemorrhages also occurred from the umbilical cord and the vagina before death. No clinical evidence of erythroblastosis was found.

*Autopsy Findings.*—Examination revealed severe jaundice of the body. The liver extended into the pelvis on the right side and weighed 375 gm. Except for jaundice throughout the body tissues, there were no abnormalities other than the enlarged liver. Microscopic sections of the

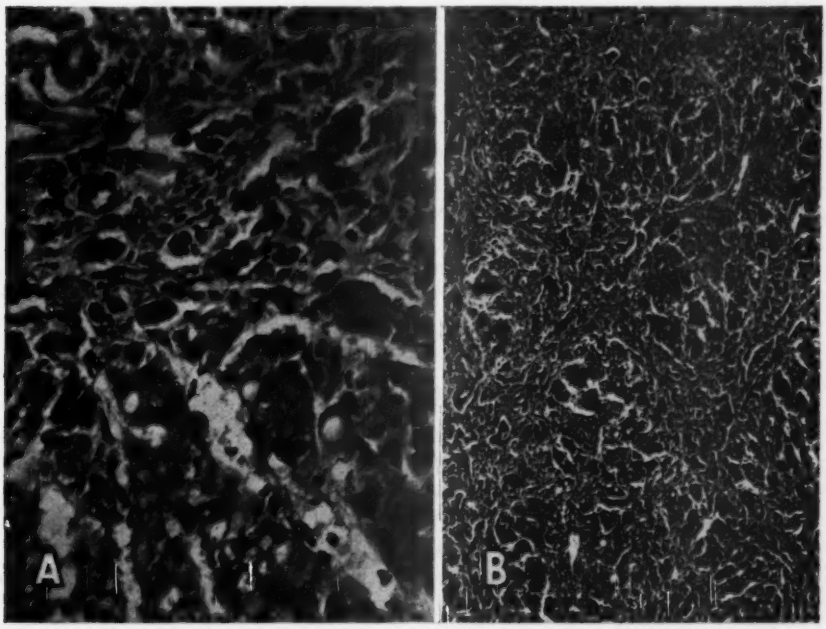


Fig. 4 (Case 4).—Photomicrographs of liver, showing the presence of bile thrombi and proliferating bile ducts somewhat resembling congenital atresia of the bile ducts. These sections do not show as much fatty metamorphosis as present in the other siblings; *A*, × 300; *B*, × 65.

liver revealed extensive fatty replacement with complete loss of normal liver structure, as seen in Figure 1*C*.

CASE 4.—The fifth pregnancy was normal, and a full-term girl was born Dec. 29, 1944. This baby also appeared normal for the first few days of life but then manifested jaundice, an enlarged liver, and bleeding from the nose and the vagina. Figure 2 shows a picture of the infant at 11 days of age when admitted to the University Hospitals. The blood cholesterol value on two occasions was 100 and 105 mg. per 100 cc. A microglucose tolerance test gave the following values: fasting, 106 mg. per 100 cc.; one hour, 140 mg. per 100 cc.; two and one-half hours, 100 mg. per 100 cc. The prothrombin time was normal. The stools were of normal color and consistency, and no free fat was observed in them. Frequent urine examinations revealed a 1-2 + albuminuria and a 1-4 + glycosuria without acetone on nearly every occasion. This sugar proved to be glucose upon fermentation testing.

The patient was treated with a low-fat, high-carbohydrate, high-protein diet, and following this it was felt that the liver receded to normal size. Soon thereafter abdominal distention due to ascites became obvious, as can be seen in Figure 3. In spite of the special diet and repeated peritoneal punctures to relieve the ascites, the illness was progressive, and the baby died on the 58th day of life.

*Autopsy Findings.*—Examination revealed marked malnutrition of the body but no evidence of jaundice. There was 600 cc. of clear amber-colored ascitic fluid present in the abdominal cavity. The absence of fat in the subcutaneous tissue and in the omentum was very noticeable. The organs appeared to be normal, except for the liver. It weighed 137 gm. and had a finely granular surface. When the liver was cut a gritty feeling was noted. Microscopic sections of the liver revealed marked proliferation of the bile ducts with bile thrombi and liver cells that contained fat droplets, as seen in Figure 4. The spleen weighed 23 gm. and appeared normal.

The following blood groups were obtained for this daughter and the remaining members of the family.

| | | | | Anti-A | Anti-B |
|---|---|---|---|---|---|
| Baby B. | A | Rh+ | M-N | 0 | 0 |
| Mother B. | O | Rh+ | M-N | 1-224 | 1-56 |
| Father B. | A | Rh— | M | ..... | .... |
| Sibling B. | A | Rh— | M | ..... | .... |

No cold agglutinins or heterophile titer was present in the sera of any of the above.

One year after the death of the fourth sibling, liver-function studies were performed on the mother and the living sibling to see if any aberration existed in them. As seen below, the results of these tests were normal.

| | Bilirubin, Mg./100 Cc. | | Thymol Turbidity, Units | Cephalin-Cholesterol | Alkaline Phosphatase, Units | Cholesterol, Mg./100 Cc. | |
|---|---|---|---|---|---|---|---|
| | 1 min. | Total | | | | Total | Ester |
| Mother B. | 0.03 | 0.2 | 2 | 1+, 48 hr. | 1.0 | 174 | 143 |
| Sibling B. | 0.06 | 0.22 | 1 | 1+, 48 hr. | 6.6 | 176 | 141 |

## COMMENT

The classification of cirrhosis in children, either by pathological criteria or by etiological factor, is difficult and complex. Nevertheless, in evaluating the familial occurrence of this disease, it is of some interest to have a classification which recognizes familial factors. The term "familial" has often been used as an equivalent of recessive inheritance, whereas it should be used only to designate the greater-than-chance occurrence of multiple cases in families. The classification given in the accompanying table indicates whether familial cases may occur, and whether or not this familial distribution may be due to hereditary factors. The classification is similar in part to that presented by Wergeland.[1]

It is important to recognize that cirrhosis may occur as a familial disease because of either environmental or hereditary factors. In only one case, hepatolenticular degeneration, does cirrhosis represent an integral part of a recognized hereditary disease. In several others, such as telangiectasia and sickle-cell anemia, cirrhosis may occur as a complication of a recognized hereditary disease. Sometimes it may occur in such conditions as bile-duct malformations and galactosemia, conditions probably dependent, at least partially, on hereditary factors.

Cases of familial cirrhosis are rather common in the medical literature. However, in several series which include all types of cirrhosis, they have represented a relatively minor fraction. No definite cases of familial cirrhosis were reported among 40

1. Wergeland, H.: On the Cause of Familial Deaths in Early Childhood, with Particular Reference to Some Uncommon Conditions, Acta. paediat. **37**:73-86, 1949.

cases by Keller and Nute [2]; three familial cases were found among 58 cases in children reported by Perozzi.[3]

The majority of reports of familial cirrhosis have dealt with juvenile nodular or atrophic cirrhosis. Some of these have been interpreted as evidence of a hereditary factor (Gutzeit and Lehman [4]). Others were interpreted as evidence of an infectious factor (Moon,[5] Schindler and Kindschi [6]). Although only familial cases are usually considered as hereditary in origin, it is necessary to suppose that some sporadic cases are of similar origin. In other words, if a disease involves either recessive or low-penetrance-dominant genes, the laws of chance will result in the

*Cirrhosis in Children*

| | Familial Occurrence | | Hereditary Factors | |
|---|---|---|---|---|
| | Possible | Reported | Definite | Probable |
| A. Primary or part of a definite entity | | | | |
| 1. Hepatolenticular degeneration | X | X | Recessive | ..... |
| 2. Juvenile atrophic cirrhosis | X | X | ..... | ? |
| 3. Idiopathic infantile cirrhosis | X | X | ..... | ? |
| B. Complicating or secondary to | | | | |
| 1. Telangiectasia | X | X | Dominant | ..... |
| 2. Galactosemia | X | X | ..... | Recessive |
| 3. Malnutrition | X | X | ..... | ..... |
| 4. Congenital malformations of the bile ducts | X | .. | ..... | ? |
| 5. Hemolytic disease | | | | |
| Sickle-cell anemia, thalassemia | X | .. | Recessives | ..... |
| Familial hemolytic jaundice | X | .. | Dominant | ..... |
| 6. Erythroblastosis | X | X | Genetic Incompatibility | ..... |
| 7. Cystic fibrosis of pancreas | X | .. | Recessive | ..... |
| 8. Congestive cirrhosis | | | | |
| Cardiac failure | .. | .. | ..... | ..... |
| Portal hypertension, thrombophlebitis of inferior vena cava, Banti's | X | X | ..... | ? |
| 9. Ulcerative colitis | .. | .. | ..... | ..... |
| 10. Infections | | | | |
| Sepsis | .. | .. | ..... | ..... |
| Acute infections, scarlet fever, etc. | X | X | ..... | ..... |
| Acute hepatitis | X | X | ..... | ..... |
| Tuberculosis | X | .. | ..... | ..... |
| Congenital syphilis | X | X | ..... | ..... |
| Parasitosis (schistosomiasis, malaria, kala-azar, ascaris, toxoplasmosis, hydatid cyst) | X | X | ..... | ..... |
| 11. Intoxicants | | | | |
| Alcohol | X | X | ..... | ..... |
| Arsenic, drugs, plant and animal poisons | X | .. | ..... | ..... |

occurrence of sporadic as well as familial cases. Thus, of Keller and Nute's 40 sporadic cases, there were 2 cases of hepatolenticular degeneration and 5 of erythroblastosis fetalis, both of which involve genetic factors; there were 5 cases of bile-duct malformations, which probably involve genetic factors. Among Perozzi's 55

2. Keller, P. D., and Nute, W. L., Jr.: Cirrhosis of the Liver in Children: Clinical and Pathologic Study of Cases, J. Pediat. **34**:588-615, 1949.

3. Perozzi, T.: Juvenile Cirrhosis, Thesis, University of Minnesota, 1938.

4. Gutzeit, K., and Lehman, W.: Die Lebercirrhosen, in Handbuch der Erbbiologie des Menschen, Berlin, Springer-Verlag, 1940, Vol. 4, Pt. 2, pp. 645-657.

5. Moon, V. H.: Atrophic Cirrhosis in Children, Am. J. Dis. Child. **46**:375-380, 1933.

6. Schindler, J. A., and Kindschi, L. G.: Juvenile Cirrhosis of Liver in 3 Members of the Same Family, Wisconsin M. J. **50**:1004, 1951.

sporadic cases there was 1 case of hepatolenticular degeneration and 11 of bile-duct malformations. In both series there were numerous cases of juvenile atrophic cirrhosis, a condition in which genetic factors are probably also important.

Cirrhosis in infants is much less common than cirrhosis in later childhood, and in general the etiologic factors are different for the two groups. In India, an infantile form of familial cirrhosis is said to be relatively common, although the exact etiology has not been determined (Wolman [7]). Heredity has been mentioned as a possible factor, although dietary factors have been considered to be most important. Fatty infiltration of the liver, possibly primary to later cirrhosis, has been described as a deficiency disease in the West Indies.[8] Infantile cirrhosis resulting from erythroblastosis and bile-duct malformations has already been mentioned. Several reports have dealt with familial infantile cirrhosis in galactosemia,[9] a metabolic disorder probably of genetic origin. Other familial cases in early infancy have been described in which the underlying factor has remained unknown, and which can best be classed as idiopathic infantile cirrhosis.

The four cases presented in this paper do not fit into any of the recognized categories of secondary cirrhosis; however, they bear considerable resemblance to several cases described by Dekker-Jonker.[10] He reported upon two sibling infants in whom diarrhea and jaundice developed several days after birth, with elevated blood-sugar levels and glucosuria; both died at less than 2 months of age, and postmortem examination revealed beginning cirrhosis: fatty degeneration of the liver, an increase in connective tissue, and proliferation of the bile ducts and bile thrombi.

The four cases presented in this paper also had many of the features of galactosemia in infants.[9b] Against this diagnosis, however, was the presence of glucose rather than galactose in the urine, absence of cataracts, and failure to do well with a low-lactose, high-protein diet.

## SUMMARY

Four infants in one sibship affected with hepatic disease leading to cirrhosis of the liver are reported upon. All died under 2 months of age, with symptoms of vomiting, jaundice, abdominal distention, and bleeding from the mucous membranes. No definite etiological factor could be identified. The etiological factors in cirrhosis are discussed, especially with respect to the familial occurrence of the disease.

The help of Dr. James S. Mc Cartney, Professor of Pathology, and Dr. Frederick W. Hoffbauer, Associate Professor of Medicine, in reviewing the pathological material and making suggestions regarding the manuscript, is acknowledged.

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10. Dekker-Jonker, A.: Over levercirrhose bij zuigelingen, Maandsch. kindergeneesk. **16**:465-469, 1949.

# HEPATIC DYSFUNCTION IN INFECTIOUS MONONUCLEOSIS IN CHILDREN

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EVIDENCE of hepatic dysfunction in infectious mononucleosis in adults has been well established. Pfeiffer,[1] in his original description of glandular fever in 1889, mentioned enlargement of the liver as one of the major physical findings in the disease. Snapper and his co-workers [2] in Europe and Downey and McKinlay [3] in this country first described the presence of jaundice in a patient with infectious mononucleosis. Wechsler and Rosenblum [4] have shown that in an epidemic of 556 cases, jaundice developed in 7.5% of the patients. Studies of pathology have confirmed the presence of liver changes in infectious mononucleosis and suggested that they are similar to those seen in viral hepatitis.[5]

Cohn and Lidman [6] first demonstrated the presence of positive results of liver-function tests in infectious mononucleosis in adults. This work has subsequently

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This study was made possible through a grant from Mead Johnson & Company.

From the Medical Service, Children's Medical Center; the Department of Pediatrics, Beth Israel Hospital, and the Department of Pediatrics, Harvard Medical School.

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6. Cohn, C., and Lidman, B. I.: Hepatitis Without Jaundice in Infectious Mononucleosis, J. Clin. Invest. **25**:145, 1946.

been confirmed by Gall,[7] DeMarsh and Alt,[8] Evans,[9] Peterson,[10] Brown,[11] Iversen,[12] Angle,[13] Bennett,[14] and Jordan,[15] all in adults. They found positive results in tests for flocculation even in the absence of jaundice.

The present study was undertaken to determine changes in results of liver-function tests in children with infectious mononucleosis.

## METHODS

The series consisted of 62 children, seen at the Children's Medical Center from 1947 to 1951, who were admitted with the presumptive diagnosis of infectious mononucleosis.

Blood smears were examined in most instances by the hematology department for abnormal cells typical of infectious mononucleosis. Heterophile determinations were done by the method of Paul and Bunnell.[16] It was felt that a heterophile titer of 1:56 or higher was diagnostic of infectious mononucleosis, and the hematological and physical findings served as supportive evidence in making the diagnosis.

The routine liver-function tests performed and the methods used[17] are given in Table 1. All of these tests can be performed on 0.5 cc. of serum or approximately 1.0 cc. of whole blood.

TABLE 1.—*Liver-Function Tests*

| Test | Method | Normal Range |
|---|---|---|
| Thymol turbidity | Maclagan [17a] | 0-4 units |
| Thymol flocculation | Neefe [17b] | 0-1+ |
| Cephalin-cholesterol flocculation | Hanger [17c] | 0-2+ at 24 hr. |
| Colloidal red | Ducci [17d] | 0-1+ |
| Cadmium sulfate | Wunderly and Wuhrman [17e] | 0 |
| Bilirubin, 1-min. reading | Malloy and Evelyn,[17f] as modified by Ducci and Watson [17g] | 0-0.2 mg./100 cc. |
| Total serum bilirubin | | 0-0.8 mg./100 cc. |

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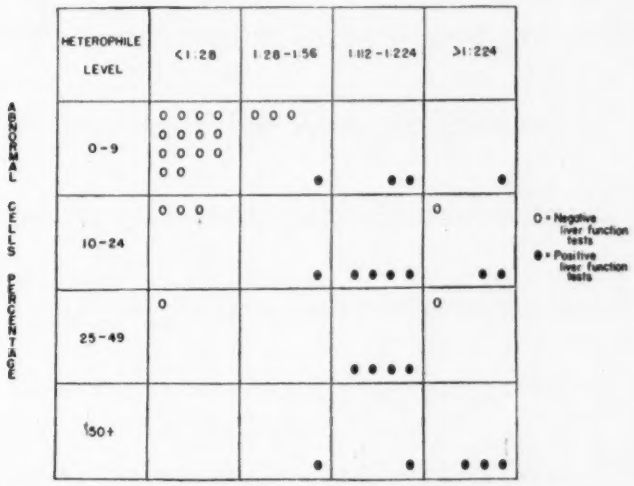
In order to obtain a long-term impression of the disease, all the children with infectious mononucleosis with positive results of flocculation tests at the time of discharge from the hospital were studied six months to four years after the onset of their disease. This was possible in 12 of 14 cases. In all these children complete physical examinations and liver-function tests were carried out at the time of follow-up study.

## RESULTS

The data on the patients were divided into three separate groups.

*Group 1.*—This group consisted of 26 patients for whom the diagnosis of infectious mononucleosis was proved by a heterophile titer of 1:56 or higher and for whom results of liver-function tests were also positive. Twenty of the 26 patients (77%) had positive hematological evidence of infectious mononucleosis, 23 of the 26 patients (89%) had hepatic enlargement, and 18 of the 26 patients (69%) had




Relation of liver-function tests to heterophile levels and abnormal cells; circles indicate negative results of liver-function tests, solid dots indicate positive results of liver-function tests.

splenic enlargement. An analysis of the liver-function tests showed that for all patients the results of one or more tests of flocculation were positive. Among the 26 patients, the results of all four liver-function tests were positive for 13 (50%), for 4 others (16%) the results of three tests were positive, and for 2 others (8%) the results of only two tests were positive. An analysis of the tests themselves show that the thymol turbidity reading was abnormal for 17 of the 26 patients tested (65%), the results of the thymol flocculation test were positive for 20 of the 26 patients tested (77%), cephalin-cholesterol flocculation was present in 19 of the 26 patients tested (73%), and the results of the colloidal red test were positive for 19

Content of Serum on the Response Given by Turbidity and Flocculation Tests, Brit. J. Exper. Path. **28**:286, 1947. (*f*) Malloy, H. T., and Evelyn, K. A.: The Determination of Bilirubin with the Photoelectric Colorimeter, J. Biol. Chem. **119**:481, 1937. (*g*) Ducci, H., and Watson, C. J.: The Quantitative Determinations of Serum Bilirubin with Special Reference to the Prompt-Reacting and the Chloroform-Soluble Types, J. Lab. & Clin. Med. **30**:293, 1945.

TABLE 2.—*Data on Sixty-Two Children in Three Groups*

| Case No. | Date | Heterophile, Titer | Abnormal Cells | Lymphadenopathy | Liver | Spleen | Thymol Turbidity, Units | Thymol Flocculation | Colloidal Red Test | Cadmium Sulfate Test | Cephalin-Cholesterol Flocculation | Serum Bilirubin, 1-Min. Reading, Mg. per 100 Cc. | Total Serum Bilirubin, Mg. per 100 Cc. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Group 1 | | | | | | | |
| 1 | 5/28/49 | 1:1792 | .... | + | 0 | + | | | | | | | |
| | 6/11/49 | 1:56 | .... | .. | .. | .. | 6.0 | 2+ | ... | 2+ | 3+ | 0.13 | 0.26 |
| 2 | 11/ 5/48 | 1:896 | Yes | + | + | + | 8.0 | 3+ | 1+ | ... | 3+ | 0.14 | 0.38 |
| 3 | 7/23/48 | 1:896 | 10% | + | + | + | 7.5 | 1-2+ | 0 | ... | 1-2+ | 0.32 | 0.51 |
| | 7/29/48 | ..... | .... | .. | .. | .. | 3.0 | ± | 0 | ± | ± | 0.09 | 0.13 |
| 4 | 11/14/49 | 1:112 | 82% | + | + | 0 | 5.0 | ± | ± | ... | 2+ | 1.76 | 2.46 |
| | 11/22/49 | 1:448 | .... | + | + | 0 | 6.0 | 2+ | 4+ | ... | 3+ | 0.06 | 0.19 |
| | 11/28/49 | ..... | 54% | .. | .. | .. | 4.5 | ± | 2+ | ... | 0 | 0.42 | 0.73 |
| | 12/22/49 | 1:112 | .... | .. | .. | .. | 2.2 | 1+ | 2+ | ... | 0 | 0.28 | 0.60 |
| | 1/16/50 | ..... | .... | .. | .. | .. | 2.5 | ± | ± | ... | 0 | 0.13 | 0.23 |
| 5 | 7/ 5/50 | 1:448 | 10-20% | + | + | + | 3.5 | 2+ | 0 | ... | 1+ | 0.06 | 0.13 |
| 6 | 12/12/49 | 1:448 | 78% | + | + | + | 2.0 | ± | 3+ | ... | 1+ | 0.09 | 0.18 |
| 7 | 5/22/50 | 1:224 | 25% | + | + | + | 4.5 | 3+ | ... | 2-3+ | 3+ | .... | .... |
| | 5/25/50 | ..... | .... | .. | .. | .. | 5.5 | 3+ | ... | 3+ | 3+ | 0.11 | 0.21 |
| | 6/ 2/50 | ..... | .... | .. | .. | .. | 3.5 | 3+ | ... | 3+ | 3+ | 0.13 | 0.24 |
| 8 | 10/14/49 | 1:448 | 5% | + | 0 | 0 | | | | | | | |
| | 10/21/49 | 1:112 | .... | .. | .. | .. | 3.0 | ± | 3.4+ | ... | 0 | 0.06 | 0.35 |
| 9 | 1/ 9/50 | 1:240 | 78% | + | 0 | + | 5.5 | 1+ | 3+ | ... | 3+ | 0.09 | 0.27 |
| 10 | 3/ 7/50 | 1:224 | 10% | + | 0 | + | 8.5 | 2+ | 2-3+ | ... | 3+ | 0.06 | 0.13 |
| | 3/21/50 | 1:224 | .... | .. | .. | .. | 8.0 | ± | ± | ... | 1-2+ | 0.06 | 0.13 |
| | 6/ 8/50 | Normal | .... | .. | .. | .. | | | | | | | |
| 11 | 1/26/48 | 1:224 | 17% | + | 0 | 0 | 4.2 | 3+ | 3+ | ... | 1-2+ | 0.06 | 0.25 |
| | 2/ 6/48 | 1:112 | .... | .. | .. | .. | 2.8 | 1+ | ± | ... | 1+ | 0.24 | 0.38 |
| 12 | 3/20/48 | 1:224 | Many | + | 0 | 0 | 5.5 | 3+ | 1+ | ... | 4+ | 0.17 | 0.27 |
| | | | | | | | 0.2 | 0 | 0 | ... | 0 | 0.08 | 0.22 |
| 13 | 3/30/51 | 1:224 | Many | + | + | + | 5.5 | 3+ | ... | ... | 3.4+ | 0.06 | 0.18 |
| | 4/ 5/51 | 1:224 | .... | .. | .. | .. | | | | | | | |
| | 4/26/51 | Normal | .... | .. | .. | .. | | | | | | | |
| 14 | 12/ 8/47 | 1:224 | 16% | .. | + | + | 4.2 | 3+ | 4+ | ... | 0 | 0.06 | 0.13 |
| 15 | 1/18/49 | 1:224 | None | 0 | 0 | 0 | 2.0 | ± | 0 | ... | 3+ | 0.11 | 0.19 |
| 16 | 6/24/48 | 1:128 | 16% | + | + | + | 2.0 | 1-2+ | ± | ... | 1+ | 0.06 | 0.13 |
| 17 | 6/ 8/49 | Normal | .... | + | 0 | + | 0.5 | 0 | 0 | ... | ± | 0.11 | 0.44 |
| | 6/14/49 | 1:32 | .... | .. | .. | .. | 2.0 | 0 | 0 | ... | 3+ | 0.06 | 0.25 |
| | 6/21/49 | 1:128 | .... | .. | .. | .. | | | | | | | |
| 18 | 3/ 9/50 | 1:112 | 6% | + | 0 | 0 | | | | | | | |
| | 3/14/50 | 1:28 | .... | .. | .. | .. | 3.0 | 1+ | 3+ | ... | 0 | 0.06 | 0.22 |
| 19 | 1/24/50 | 1:112 | Yes | + | 0 | 0 | 3.0 | 2+ | ... | ± | 1+ | 0.06 | 0.19 |
| | | | | | | | 3.0 | 1+ | ... | ± | ± | 0.19 | 0.35 |
| 20 | 12/26/47 | 1:112 | 62% | + | + | + | 1.8 | 0 | ± | ... | 2+ | 0.08 | 0.35 |
| 21 | 4/15/48 | 1:112 | 30% | + | + | + | 3.8 | 2+ | 1+ | ... | 3+ | 0.19 | 0.44 |
| | 4/21/48 | ..... | .... | .. | .. | .. | 4.5 | 2+ | ± | ... | 1+ | 0.09 | 0.25 |
| | 5/ 5/48 | ..... | .... | .. | .. | .. | 1.2 | 0 | 0 | ... | ± | 0.15 | 0.38 |
| 22 | 4/ 4/49 | 1:56 | None | + | 0 | + | 3 | 3+ | 3+ | ... | 3+ | 0.06 | 0.61 |
| | 4/18/49 | 1:112 | .... | .. | .. | .. | 7.5 | 3+ | 3+ | ... | 3+ | 0.06 | 0.25 |
| 23 | 12/26/50 | 1:112 | .... | .. | .. | .. | 13.0 | 3-4+ | ... | VS+ | 3+ | 0.72 | 1.27 |
| | 1/24/51 | ..... | .... | .. | .. | .. | 11.0 | 3-4+ | ... | ... | 2-3+ | 0.19 | 0.67 |
| 24 | 11/16/48 | 1:56 | 2 | + | + | + | 8.0 | 3+ | 1+ | ... | 3+ | 0.08 | 0.25 |
| | 11/29/48 | 1:56 | .... | .. | .. | .. | 6.0 | 3-4+ | 3+ | ... | ... | .... | .... |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 25 | 6/24/49 | 1:56 | 11% | + | + | + | 2.0 | 3+ | 2+ | ... | 3+ | 0.06 | 0.13 |
| 26 | 11/ 6/47 | 1:56 | 55% | + | + | + | 8.5 | 3+ | 3+ | ... | 3+ | 0.14 | 0.28 |
| | 11/14/47 | ..... | .... | .. | .. | .. | 7.0 | 3+ | 4+ | ... | 3+ | 0.19 | 0.22 |
| | 11/26/47 | ..... | .... | .. | .. | .. | 5.5 | 3+ | 4+ | ... | 2+ | 0.19 | 0.23 |
| | 12/ 2/47 | ..... | .... | .. | .. | .. | 4.0 | 2+ | 3+ | ... | ± | 0.11 | 0.38 |
| | 12/11/47 | ..... | .... | .. | .. | .. | 3.5 | 2+ | 3+ | ... | ± | 0.14 | 0.41 |
| | | | | | | Group 2 | | | | | | | |
| 27 | 6/23/49 | 1:896 | 19% | + | 0 | 0 | 3.5 | ± | 1+ | ... | ± | 0.16 | 0.32 |
| 28 | 3/ 9/50 | 1:896 | 45% | + | + | + | | | | | | | |
| | 3/20/50 | ..... | .... | .. | .. | .. | 1.2 | 0 | 0 | ... | 0 | 0.06 | 0.13 |
| 29 | 9/ 2/49 | 1:224 | .... | + | + | 0 | 2.0 | 0 | 0 | ... | 0 | 0.01 | 0.38 |
| | 10/ 3/49 | 1:14 | .... | .. | .. | .. | 0.8 | 0 | 0 | ... | 0 | 0.08 | 0.28 |
| 30 | 10/23/50 | 1:224 | None | + | + | + | 1.5 | 0 | 0 | 0 | 0 | 0.06 | 0.18 |
| 31 | 12/22/50 | 1:112 | .... | + | 0 | 0 | | | | | | | |
| | 1/11/51 | 1:112 | .... | .. | .. | .. | 2.0 | 0 | ... | 0 | 1+ | 0.09 | 0.22 |
| | | | | | | Group 3 | | | | | | | |
| 32 | 10/ 6/50 | 1:28 | None | + | + | + | | | | | | | |
| | 10/20/50 | ..... | .... | .. | .. | .. | 0.5 | 0 | 0 | ... | ± | 0.06 | 0.13 |
| 33 | 6/ 1/49 | 1:28 | None | + | 0 | 0 | 0.8 | 0 | 0 | ... | 0 | 0.17 | 0.38 |
| 34 | 6/21/50 | 1:28 | Yes | + | 0 | 0 | 1.8 | 0 | 0 | ... | 1+ | 0.06 | 0.8 |
| 35 | ..... | ..... | .... | .. | .. | .. | 2.5 | 0 | ± | ... | 1+ | 0.06 | 0.13 |
| | 9/25/50 | 1:28 | None | + | + | + | 1.2 | 0 | 0 | ... | 2+ | 0.17 | 0.67 |
| 36 | 10/21/49 | 1:14 | .... | + | 0 | 0 | 1.0 | 0 | 1-2+ | ... | 0 | 0.06 | 0.19 |
| 37 | 6/26/50 | 1:14 | 4% | + | 0 | + | 1.2 | 0 | 0 | ... | 0 | 0.06 | 0.13 |
| 38 | 11/ 4/47 | 1:14 | 32% | + | 0 | 0 | 1.8 | ± | 0 | ... | 1+ | 0.06 | 0.35 |
| 39 | 10/17/49 | 1:7 | None | + | 0 | 0 | 3.0 | 0 | 0 | ... | 0 | 0.06 | 0.13 |
| 40 | 4/20/50 | 1:7 | Occasional | + | + | + | 1.5 | 0 | 0 | ... | ± | 0.11 | 0.31 |
| 41 | 8/30/50 | Normal | None | + | 0 | 0 | | | | | | | |
| | 9/ 6/50 | ..... | .... | .. | .. | .. | 0.5 | 0 | 0 | ... | 0 | 0.06 | 0.13 |
| 42 | 3/12/51 | Normal | None | 0 | 0 | 0 | 0.5 | 0 | ... | ... | 0 | 0.26 | 0.42 |
| 43 | 9/11/50 | Normal | 6% | + | 0 | + | 1.0 | 0 | 2+ | ... | ... | 0.06 | 0.13 |
| 44 | 10/28/49 | Normal | None | + | 0 | 0 | 1.2 | 0 | 0 | ... | 0 | 0.09 | 0.25 |
| 45 | 11/16/50 | Normal | None | 0 | 0 | 0 | 1.8 | 0 | 0 | ... | 0 | 0.08 | 0.18 |
| 46 | 1/17/50 | Normal | None | + | 0 | 0 | 0.2 | 0 | 0 | ... | 0 | 0.11 | 0.31 |
| 47 | 11/22/50 | Normal | 14% | + | 0 | + | 0.2 | 0 | ... | 0 | 0 | 0.11 | 0.22 |
| 48 | 5/ 5/50 | Normal | None | + | 0 | 0 | 1.5 | 0 | 0 | ... | ± | 0.06 | 0.13 |
| 49 | 3/26/51 | Normal | None | + | 0 | 0 | 1.2 | 0 | ... | ... | ... | 0.08 | 0.21 |
| | 4/ 8/51 | Normal | .... | .. | .. | .. | | | | | | | |
| 50 | 10/ 5/50 | Normal | Yes | + | 0 | 0 | 0.2 | 0 | 0 | ... | 0 | 0.06 | 0.13 |
| 51 | 1/19/50 | Normal | .... | + | .. | 0 | 2.0 | 1-1 | ... | + | 2+ | 0.06 | 0.13 |
| 52 | 11/21/50 | Normal | 15% | + | 0 | 0 | 1.0 | 0 | ... | 0 | 2+ | 0.25 | 0.47 |
| 53 | 1/22/51 | Normal | 2% | + | + | + | 1.2 | 0 | ... | ... | 2+ | 0.06 | 0.13 |
| | 2/ 6/51 | Normal | .... | .. | .. | .. | 0.7 | 0 | ... | ... | ± | 0.08 | 0.13 |
| 54 | 6/28/48 | Normal | 20% | + | 0 | 0 | 0.5 | 0 | 0 | ... | ± | 0.21 | 0.61 |
| 55 | 6/18/48 | Normal | 19% | + | 0 | 0 | 0.2 | 0 | 0 | ... | 1+ | 0.09 | 0.28 |
| 56 | 9/23/50 | None | .... | + | 0 | 0 | 1.0 | 0 | 0 | ... | 0 | 0.06 | 0.13 |
| 57 | 11/21/49 | None | 4% | 0 | 0 | 0 | 1.2 | 0 | 0 | ... | ± | 0.06 | 0.13 |
| 58 | 9/28/49 | None | .... | + | 0 | 0 | 3.2 | 0 | 0 | ... | ± | 0.08 | 0.70 |
| 59 | 3/14/50 | None | .... | 0 | 0 | 0 | 0.8 | 0 | 0 | ... | 0 | 0.06 | 0.13 |
| 60 | 10/19/50 | None | .... | 0 | 0 | 0 | 1.2 | 0 | 0 | ... | ± | 0.22 | 0.57 |
| 61 | 4/28/48 | Normal | None | + | 0 | + | 3.5 | ± | 0 | ... | 0 | 0.08 | 0.13 |
| 62 | 3/19/48 | None | .... | + | 0 | 0 | 0.9 | 0 | ± | ... | ± | 0.06 | 0.12 |

of the 22 patients tested (86%). The serum bilirubin levels were within normal limits in all except the patient in Case 4, in whom a clinical hepatitis associated with infectious mononucleosis developed.

CASE 4 (352702).—The patient was an 8½-year-old white girl who was admitted with the chief complaint of abdominal pain, nausea, vomiting, and fever.

*Present Illness.*—She had a low-grade fever for 10 days prior to admission. Four days before admission marked anorexia developed, and two days before admission the patient had persistent nausea and vomiting. She had complained of slight intermittent abdominal pain localized in both lower quadrants. For two days prior to admission the urine was scant and dark.

*Physical Examination.*—The temperature was 102 F., the pulse rate 108, and the respirations 30 per minute. The patient appeared well developed and well nourished and was not acutely ill. There was no jaundice of the sclerae or skin. There was a spider hemangioma over the right lower lid. There was no generalized lymphadenopathy. The liver was tender and palpable 4 cm. below the costal margin. The spleen was not palpable.

*Laboratory Data.*—The urine contained bile initially, but this cleared up one week later, and upon discharge only urobilinogen in normal amounts was found in the urine. The hemoglobin level was 11.8 gm., the red blood cell count was 3,940,000, and the white blood cell count was 5,900, with 80% lymphocytes, typical of infectious mononucleosis. The heterophile titer, which was 1:112 upon admission, rose at the end of the first week to 1:448. The sedimentation rate was 36 mm. per hour. The reactions to a test with old tuberculin and to a Hinton test for syphilis were negative. The results of liver-function tests upon admission were as follows: thymol turbidity, 5.0 units; thymol flocculation, ±; colloidal red, ±; cephalin-cholesterol flocculation, 2+; one-minute reading for bilirubin, 1.76 mg. per 100 cc., and total serum bilirubin, 2.46 mg. per 100 cc. One week later the tests showed the following results: thymol turbidity, 6.0 units; thymol flocculation, 2+; colloidal red, 4+; cephalin-cholesterol flocculation, 3+; one-minute reading for bilirubin, 0.06 mg. per 100 cc., and total serum bilirubin, 0.19 mg. per 100 cc. Subsequently, the results of the liver-function tests reverted to normal in six weeks.

*Course in the Hospital.*—The temperature returned to normal with bed rest and a regimen of high-protein, high-carbohydrate diet, vitamins, liver extract, and aureomycin for 10 days. On the second hospital day the spleen became palpable; on the fourth day icterus of the sclerae was noted; on the fifth day the liver was less palpable, and the spleen could not be felt. There was less bile in the urine.

*Discharge Diagnosis.*—The diagnosis at the time of discharge was infectious mononucleosis, acute, with hepatitis.

*Group 2.*—This group consisted of five patients who had a high heterophile titer and clinical evidence of infectious mononucleosis but who did not show definitely positive results of liver-function tests. In cases 27 and 31 there were some borderline changes, but these were not considered sufficient to permit a diagnosis of liver dysfunction.

*Group 3.*—This group consisted of 31 patients who were sent to the Children's Medical Center with the presumptive diagnosis of infectious mononucleosis. The diagnosis was subsequently discarded because the results of heterophile tests and of hematologic studies were negative and because the clinical course was considered incompatible with a diagnosis of infectious mononucleosis. Liver-function tests were done on these patients as an added diagnostic tool and results of these were all negative. It is conceivable that some of these patients had mild cases of infectious mononucleosis, but the evidence was insufficient to establish the diagnosis.

The over-all results are shown in Table 3. It can be seen that 84% of the patients with definite infectious mononucleosis according to heterophile titer showed positive results of liver-function tests. Similarly, all the patients who were admitted with the presumptive diagnosis of infectious mononucleosis but who eventually proved not to have the disease had negative results in liver-function tests. In the accompanying chart the relationship of heterophile levels, abnormal-cell percentages, and results of liver-function tests are plotted. It is evident that the results of liver-

TABLE 3.—*Sixty-Two Patients with Admission Diagnosis of Infectious Mononucleosis*

| Heterophile Titer | Results of Liver-Function Tests | | Total |
|---|---|---|---|
| | Positive | Negative | |
| 1:56 or higher | 26 (84%) | 5 (16%) | 31 |
| Less than 1:56 | 0 | 31 (100%) | 31 |

TABLE 4.—*Follow-Up Data of Twelve Children Showing Flocculation at Time of Discharge*

| Case No. | Follow-Up Study, Yr. | Clinical Status | | Liver Function | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Thymol Turbidity, Units | Thymol Flocculation | Cephalin-Cholesterol Flocculation | Serum Bilirubin, 1-Min. Reading, Gm. per 100 Cc. | Total Serum Bilirubin, Gm. per 100 Cc. |
| 13 | 7½ mo. | Well | Before | 5.5 | 3+ | 3-4+ | 0.06 | 0.18 |
| | | | Follow-up | 5.0 | 2+ | 2-3+ | 0.09 | 0.25 |
| 23 | 8¾ mo. | Well | Before | 11.0 | 3-4+ | 2-3+ | 0.19 | 0.67 |
| | | | Follow-up | 7.5 | 2-3+ | ± | 0.25 | 0.81 |
| 18 | 1½ | Well | Before | 3.0 | 1+ | 0 | 0.06 | 0.22 |
| | | | Follow-up | 5.0 | 1+ | ± | 0 | 0 |
| 1 | 2½ | Intolerance to fatty foods | Before | 6.0 | 2+ | 3+ | 0.13 | 0.26 |
| | | | Follow-up | 2.0 | 1+ | ± | 0 | 0 |
| 22 | 2½ | Well | Before | 7.5 | 3+ | 3+ | 0.06 | 0.25 |
| | | | Follow-up | 5.0 | 1-2+ | 2-3+ | 0.13 | 0.31 |
| 25 | 2½ | Well | Before | 9.0 | 3+ | 3+ | 0.06 | 0.13 |
| | | | Follow-up | 5.0 | 2+ | 2-3+ | 0.09 | 0.25 |
| 17 | 2½ | Well | Before | 2.0 | 0 | 3+ | 0.06 | 0.25 |
| | | | Follow-up | 4.0 | ± | ± | 0 | 0.12 |
| 24 | 3 | Well | Before | 6.0 | 3-4+ | 3+ | 0.08 | 0.25 |
| | | | Follow-up | 2.5 | 2+ | 2+ | 0.13 | 0.25 |
| 2 | 3 | Vomiting and headaches | Before | 8.0 | 2+ | 3+ | 0.14 | 0.38 |
| | | | Follow-up | 1.5 | 0 | 0 | Normal | |
| 15 | 3 | Well | Before | 2.0 | ± | 3+ | 0.11 | 0.19 |
| | | | Follow-up | 2.0 | 1+ | 1+ | 0.09 | 0.18 |
| 14 | 4 | Well | Before | 4.2 | 3+ | 0 | 0.06 | 0.13 |
| | | | Follow-up | 3.0 | ± | 3+ | 0.13 | 0.50 |
| 20 | 4 | Well | Before | 1.8 | 0 | 2+ | 0.08 | 0.35 |
| | | | Follow-up | 1.0 | ± | 2-3+ | 0 | 0.37 |

function tests tend to become more strongly positive as the heterophile level and abnormal-cell percentage rise.

## FOLLOW-UP STUDY

The follow-up data on 12 of 14 children who showed positive results of tests for flocculation at the time of discharge from the hospital are given in Table 4. It can be seen that 4 of the 12 patients still show flocculation. The patients in cases 13 and 23 have been followed for only seven and eight months following the acute disease, but the patients in cases 22 and 25 have been followed for 2½ years after the disease. Clinically, all of the children, including the four still showing flocculation, are well. None of them shows enlarged lymph nodes or hepatosplenomegaly, nor has any had

relapse or jaundice following the acute episode of the disease. One child has complained of intolerance to fatty foods, and another has occasional migraine-like headaches and vomiting. Neither of these children show flocculation, and these complaints are probably unrelated to infectious mononucleosis.

## COMMENT

The correlation of liver-function tests with heterophile studies in infectious mononucleosis in children is complicated by a number of factors. Paul and Bunnell [16] have stated that the heterophile test is based upon the pattern of serum proteins, which is more frequently altered in children than in adults because of immunizations and infections, and hence the test is less accurate. The normal values for the various liver-function tests in children and the factors that alter these values are as yet largely unknown because of the limited experience of most laboratories with these tests for children. Finally, from a number of these patients only one blood specimen was taken initially, and this may not have been obtained at the optimal time to demonstrate either the heterophile rise or the liver-function changes.

Despite these limitations, the data obtained appear to be similar to the findings of various studies on adults. Gall [7] showed changes in 39 of 44 cases of proved infectious mononucleosis. Evans [9] reported cephalin-cholesterol flocculation in 90% of his patients. Peterson [10] showed that 55% of his patients showed moderate to severe hepatic dysfunction. Brown [11] obtained liver-function changes in 73 to 75% of his patients. The results are not as consistent as those of Cohn and Lidman [6] and DeMarsh and Alt [8] who obtained 100% correlation.

The diagnosis of infectious mononucleosis in infants and children is frequently important because of the differential diagnosis with leukemia and tonsillitis or other infections. In view of the fact that the heterophile titer may be slow in rising or may never rise at all, and since the other usual diagnostic methods are not satisfactory, it appears that liver-function tests may prove to be a valuable aid in confirming the diagnosis. The tests discussed in this paper can be done easily and economically with small quantities of blood in most clinical laboratories.

It should be borne in mind, however, that the so-called liver-function tests should be used only as an aid in the diagnosis of infectious mononucleosis and not as the sole test. The results have demonstrated that false-negative results may occur if specimens are not drawn at the optimal time. Also it is known that various diseases may alter the tests and give rise to false-positive results.

This study confirms the impression of several authors [18] that no one liver-function test appears to be more specific than another in the demonstration of liver dysfunction in infectious mononucleosis. Also, there appears to be no definite correlation between the changes in heterophile levels and the changes in results of liver-function tests during the illness in any individual patient. This study shows that in children, as in adults, the signs of liver dysfunction are nonspecific and that one cannot by liver-function tests alone differentiate between this disease and infectious hepatitis. This is not surprising in view of the similarity of the electrophoretic pattern of the serum of the patients with these diseases, as shown by Sterling.[19] It is important also

18. Custer and Smith.[8h] Gall.[7] Evans.[9] Peterson.[10] Brown and others.[11]

19. Sterling, K.: Serum Proteins in Mononucleosis, J. Clin. Invest. **28**:1057, 1949.

to emphasize that every patient with a diagnosis of infectious hepatitis should have heterophile studies performed to rule out infectious mononucleosis. The heterophile titer does not become abnormal in infectious hepatitis.

It is still not clear as to whether patients with infectious mononucleosis who show flocculation are suffering from a diffuse hepatitis or whether the disease in some way alters the serum proteins in the patient without giving rise to a hepatitis. Studies of pathology in a few adults show that the lesions in the liver are not dissimilar to those seen in viral hepatitis. Leibowitz [5k] has reported upon a patient who progressed from hepatitis associated with infectious mononucleosis to frank cirrhosis as proved by biopsy. Despite this suggestive evidence that positive results of liver-function tests may be due to a diffuse hepatitis, the vast majority of patients with infectious mononucleosis do not demonstrate the severe clinical symptoms of hepatitis, and all seem to make rapid and complete clinical recoveries, as opposed to the relatively high incidence of clinical recurrences and relapses reported in infectious hepatitis.[20] It would be of interest to attempt to correlate persistence of positive results in adults who complain of easy fatigability and incapacity following apparent recovery from the acute stage of infectious mononucleosis. The paucity of symptoms in children with the disease and its milder clinical course make such a correlation in children impossible.

Since the significance of the positive results of liver-function tests is still not clear, and since both Bennett [14] and the present study show that positive results of liver-function tests may persist for long periods after the end of the active disease, it would appear wise until more information is available to regard the hepatitis of infectious mononucleosis as the same type of inflammatory process as infectious hepatitis. The treatment of these patients should, therefore, be similar to that used against infectious hepatitis, with specific emphasis on longer bed rest, reduced physical activity after ambulation, and high-caloric and high-vitamin diets. This type of therapy appears to be especially indicated for patients with clinical jaundice, as in case 4, and for patients who show persistent positive results of liver-function test, as in cases 13, 23, 22, and 25.

## SUMMARY

In a study of 62 children with a presumptive diagnosis of infectious mononucleosis, 84% of the patients with a heterophile titer of 1 : 56 or higher showed positive results of liver-function tests.

In the same study, all the patients who were admitted with the presumptive diagnosis of infectious mononucleosis but who subsequently proved not to have the disease showed negative results of liver-function tests.

It is suggested that liver-function tests should be used as an addition to the diagnostic methods used for infectious mononucleosis in children.

In view of the persistence of flocculation in 4 of 12 children with infectious mononucleosis when followed up at considerable intervals, and in view of the pathological similarity between infectious mononucleosis and infectious hepatitis, it would appear advisable, at least for the present, to treat such children as if they had diffuse hepatitis.

20. Post, J.; Gellis, S., and Lindenauer, A. J.: Studies on the Sequelae of Acute Infectious Hepatitis, Am. Int. Med. **33**:1378, 1950.

# PERTUSSIS

## Treatment with Aureomycin; Clinical Study of Eighty-Five Patients and Seventy-Four Controls

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RECENT reports in the medical literature suggest that aureomycin might be effective in the treatment of pertussis. At the present time there is much to be desired in the treatment of pertussis even with the drugs now available. Many reports have been made on the benefits of human and rabbit antipertussis serum, the sulfonamides, pertussis vaccine, ascorbic acid, penicillin, polymyxin B, and streptomycin.[1] The search for a more effective therapeutic agent continues. Many of the antibiotics heretofore recommended for the treatment of pertussis are highly effective against Hemophilus pertussis in vitro but not in vivo. Aureomycin has been reported recently [2] to be effective in the treatment of pertussis. Most of the reports are based upon observations of small series of patients, and many of the studies lack parallel control.

The purpose of this study is to compare the course of pertussis in patients treated with aureomycin with the course of the disease in patients receiving symptomatic and supportive treatment.

### MATERIAL AND METHODS

Each pertussis patient was assigned alternately and without selection to one of two groups upon admission to the Philadelphia Hospital for Contagious Diseases, from October, 1949, to October,

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From the Philadelphia Hospital for Contagious Diseases.

Aureomycin was supplied by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

1. Bradford, W. L.; Day, E., and Berry, G. P.: Improvement of the Nasopharyngeal Swab Method of Diagnosis in Pertussis by the Use of Penicillin, Am. J. Pub. Health. **36**:468, 1946. Echandia, R. G.: Treatment of Whooping Cough with Streptomycin, Pediat. Américas **7**:142, 1949. Gordon, V. H., and Almaden, P. J.: Streptomycin Therapy for Pertussis, J. Pediat. **34**:279, 1949. Leichenger, H., and Schultz, A.: Streptomycin in the Treatment of Pertussis, ibid. **33**:552, 1948. Wannamaker, L. W.; Kohn, J. L., and Weichsel, M.: Streptomycin in the Treatment of Whooping Cough, Am. J. Dis. Child. **78**:201, 1949. Schwabacher, H.; Wilkinson, R. H., and Karran, C. W. C.: Streptomycin in Whooping Cough, Lancet **1**:180, 1949. Kaplan, S.; Fischer, A. E., and Kohn, J. L: Treatment of Pertussis with Polymyxin B (Aerosporin), J. Pediat. **35**:49, 1949.

2. Barbera, L., and Marchese, G.: Aureomycin and Chloramphenicol in the Treatment of Whooping Cough, Pediatria **58**:177, 1950. Chang, S.-M.; Wells, E. B.; Place, E. H., and Finland, M.: Aureomycin Treatment of Pertussis, J. Pediat. **36**:443, 1950. Bell, J. A.; Pittman, M. P., and Olson, B. J.: Pertussis and Aureomycin, Pub. Health Rep. **64**:589, 1949.

1950. There were admitted into the control group 12 patients in the first week of disease, 22 patients in the second week, 31 patients in the third week, and 9 patients in the fourth week. In the aureomycin group 11 patients were admitted in the first week, 37 patients in the second week, 28 patients in the third week, and 19 patients in the fourth week.

For each patient a nasopharyngeal culture for H. pertussis was made on penicillin-treated Bordet-Gengou medium upon admission, and a complete blood count and a roentgenogram of the lungs were done. The diagnosis of pertussis was made on the basis of a positive nasopharyngeal culture or lymphocytic leucocytosis in addition to a definite clinical picture of pertussis.

Patients in the control group received supportive treatment which comprised nasopharyngeal aspirations and administration of antipyretics, oxygen, parenteral fluids, blood transfusions, sedatives, penicillin, streptomycin, or sulfadiazine as indicated. Each patient in this group received 50 mg. per kilogram of body weight daily of an encapsuled yellow lactose powder every four hours for 10 days. Thirty-four patients in this group received no antibiotic, 26 received penicillin, 6 received penicillin and streptomycin, 5 received penicillin and sulfadiazine, 2 received sulfadiazine, and 1 received penicillin, streptomycin, and sulfadiazine.

TABLE 1.—*Distribution of Patients According to Age and Treatment*

| | Treatment of Control Patients | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Age, Yr. | No Antibiotic | Penicillin | Penicillin, Streptomycin | Penicillin, Sulfadiazine | Sulfadiazine | Sulfadiazine, Streptomycin, Penicillin | Total | Aureomycin-Treated Patients |
| 0-5 mo. | 18 | 6 | 4 | 2 | 1 | 0 | 31 | 40 |
| 6-11 mo. | 3 | 7 | 2 | 0 | 1 | 0 | 13 | 15 |
| 1 | 5 | 4 | 0 | 2 | 0 | 1 | 12 | 12 |
| 2 | 4 | 6 | 0 | 1 | 0 | 0 | 11 | 4 |
| 3 | 1 | 2 | 0 | 0 | 0 | 0 | 3 | 8 |
| 4 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| 6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| 7 | 2 | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 |
| 9 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 |
| | 34 | 26 | 6 | 5 | 2 | 1 | 74 | 85 |

The patients in the aureomycin group were provided the same nursing care, and, except for receiving 50 mg. of aureomycin per kilogram of body weight daily in four hourly doses orally for 10 days, they were treated in the same manner.

All patients previously immunized or who received antipertussis serum before admission were excluded from the statistical study The distribution of the patients according to age and treatment is shown in Table 1.

Tally sheets were kept at the bedside for the nursing staff to tabulate the number of paroxysms, attacks of cyanosis or apnea, nasopharyngeal aspirations required, and flushings of the face as these events occurred.

In the analysis of the data each event was weighted according to its seriousness or severity and frequency. The range of the number of paroxysms for each week was from 0 to 143 and was assigned a value ranging from 0 to 6. Severity of the paroxysms was rated as 1 for mild, 3 for moderately severe, and 5 for severe. The frequency of facial flushing or mild cyanosis occurred from 0 to 108 times weekly and was rated from 0 to 7, cyanosis or apnea was rated from 0 to 9, emesis was rated from 0 to 4, and the number of nasopharyngeal aspirations, from 0 to 7. The sum of the values for each week was designated as the severity index for that period for the patient. The average of severity indices of the patients for each specific period, designated as the mean severity index, compares favorably with the mean frequency of the paroxysms. The

mean severity index, however, is considered to be more representative of the clinical course of the disease than is the mean (Fig. 1) number of paroxysms.

## RESULTS

For each week's period the mean severity index of 85 patients in the aureomycin group was compared with the mean severity index of 74 patients in the control group (Fig. 1*A*). The course of the disease in the control group, which presumably represents the natural course of the disease, reaches its fastigium in the second

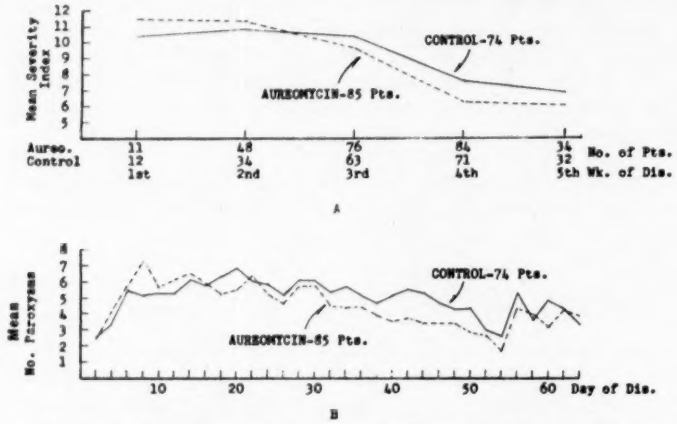


Fig. 1.—Comparison of course of pertussis in the aureomycin-treated group with the control group according to mean severity index and daily mean paroxysms.

TABLE 2.—*Comparison of the Mean Severity Indices of All Cases of Pertussis in the Aureomycin Group with Those of the Control Group*

| | Aureomycin | | | | Control | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Week | M. S. I.* | Patients, No. | SDm† | SEm‡ | M. S. I. | Patients, No. | SDm | SEm | SE Diff.m§ |
| 1 | 11.5 | 11 | 3.7 | 1.1 | 10.3 | 12 | 6.6 | 1.9 | 2.2 |
| 2 | 11.4 | 48 | 4.8 | 0.7 | 10.8 | 34 | 6.0 | 1.0 | 1.2 |
| 3 | 9.6 | 76 | 5.4 | 0.6 | 10.4 | 63 | 5.2 | 0.7 | 0.9 |
| 4 | 6.3 | 84 | 4.6 | 0.5 | 7.6 | 71 | 5.1 | 0.6 | 0.8 |
| 5 | 6.1 | 34 | 4.2 | 0.7 | 6.9 | 32 | 4.4 | 0.8 | 1.1 |

* Mean severity index.
† Standard deviation of mean.
‡ Standard error of mean.
§ Standard error of difference of means.

week then slowly regresses in the ensuing weeks. Recession of the disease in the aureomycin group of patients begins at the onset and occurs at a slightly more rapid rate than in the control group. A statistical analysis of the results in both groups indicates that this difference is not statistically significant (Table 2).[3]

3. The standard error of the mean and the standard error of the difference between the means were obtained by the methods presented by Hill, A. B.: Principles of Medical Statistics, Ed. 4, London, The Lancet Limited, 1948. If the difference between the observed difference of the means is more than 3 standard errors, the difference is significant; if the difference is more than 2 but less than 3 standard errors, the difference is probably significant.

Except for greater severity and absence of fastigium in the second week, the pattern of the disease in the patients under one year of age in the control group is similar to the course of the disease for all patients in the control group (Fig. 1*A* and Fig. 2). The course of the disease in patients under one year of age in the aureomycin group parallels the course of the disease for all patients in the aureomycin group. A comparison of the mean severity indices of both groups for patients under one year old, however, indicates that the more rapid regression of the disease in the aureomycin group, though not marked, is apparent in the third week of disease.

The course of pertussis in the aureomycin and control groups appears to be similar when treatment is started after the first week of disease (Fig. 3). However, when treatment is started in the first week of disease, regression of the disease

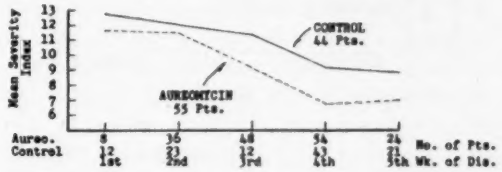


Fig. 2.—Comparison of the course of pertussis in patients under one year old in the aureomycin-treated and control groups.

TABLE 3.—*Comparison of the Mean Severity Indices of Pertussis Patients Under One Year Old with Those of the Control Group*

| | Aureomycin | | | | Control | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Week | M. S. I.* | Patients, No. | SD† | SEm‡ | M. S. I. | Patients, No. | SD | SEm | SE Diff.m§ |
| 1 | 11.6 | 8 | 4.2 | 1.5 | 12.8 | 12 | 6.7 | 1.9 | 2.4 |
| 2 | 11.5 | 36 | 4.9 | 0.8 | 12.0 | 23 | 5.8 | 1.2 | 1.4 |
| 3 | 9.1 | 48 | 5.7 | 0.8 | 11.9 | 42 | 5.2 | 0.8 | 1.1 |
| 4 | 6.8 | 54 | 4.9 | 0.7 | 9.1 | 43 | 5.0 | 0.8 | 1.1 |
| 5 | 7.0 | 24 | 3.9 | 0.8 | 8.9 | 21 | 4.0 | 0.9 | 1.2 |

* Mean severity index.
† Standard deviation of mean.
‡ Standard error of mean.
§ Standard error of difference of means.

appears to be more rapid in the aureomycin group than in the control group. The number of cases treated in the first week of disease is too small to permit definite conclusions, however.

The influence of pneumonia on the course of pertussis was studied. There were 14 patients with bronchopneumonia in each group. Twelve of the patients with pneumonia in the control group and 11 of the pneumonia patients in the aureomycin group were admitted in the second and third weeks of pertussis. The course of pertussis bronchopneumonia is shown in Figure 4*B*. The improvement is less erratic in the aureomycin-treated patients, otherwise the difference in the two groups is not remarkable. The number of cases in this category is again too small for reliable statistical evaluation.

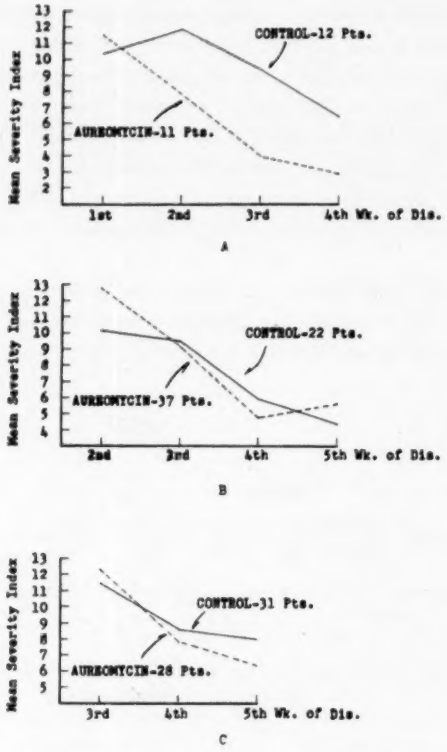


Fig. 3.—Course of pertussis according to the week of disease when treatment was started.

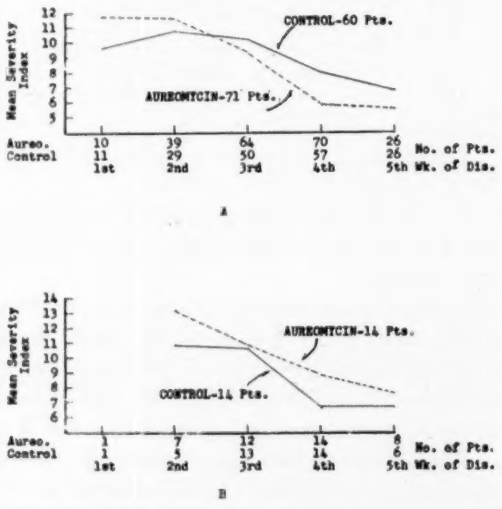
Mean Severity Index
CONTROL-60 Pts.
AUREOMYCIN-71 Pts.
Aureo. 10 39 64 70 26
Control 11 29 50 57 26 No. of Pts.
1st 2nd 3rd 4th 5th Wk. of Dis.
A
AUREOMYCIN-14 Pts.
CONTROL-14 Pts.
Aureo. 1 7 12 14 8
Control 1 5 13 14 6 No. of Pts.
1st 2nd 3rd 4th 5th Wk. of Dis.
B

Fig. 4.—Comparison of course of pertussis; *A*, without pneumonia; *B*, with pneumonia.

There were three deaths (1.8%) in the entire series. Two (2.3%) of the deaths occurred in the aureomycin group and were caused by pneumonia and by apnea. One (1.4%) death in the control group was caused by cardiac failure.

### UNTOWARD REACTIONS AND TREATMENT FAILURES

Emesis and diarrhea occurred in six patients (6.9%), but medication had to be discontinued in only two patients.

There were 10 patients who were considered aureomycin failures, in that medication had to be discontinued because of untoward reactions and apparent ineffectiveness. Two of these patients, who received aureomycin one and three days, respectively, were assigned to the control group. The remaining eight patients received aureomycin longer than three days, two for a full course and one for two full courses. These patients were included in the aureomycin group. The condition of the first patient, with pertussis and pneumonia, became worse after admission to the hospital in spite of five days' treatment with aureomycin. The pneumonia improved markedly with penicillin, even though a coliform bacillus was isolated by nasopharyngeal culture. The second patient, with pertussis and otitis media, manifested diarrhea, a temperature of 104 F., and acidosis ($CO_2$ 16 vol. %). On the sixth day, penicillin and sulfadiazine were substituted for aureomycin, with abatement of the symptoms. The third patient, with pertussis and suppurative otitis media, had a persistent temperature of 104 F. and no improvement in the otitis media in spite of a myringotomy. He recovered from the otitis media after penicillin was used, on the 4th day, although a second myringotomy was required. A fourth child, with pertussis and suppurative otitis media, did not show improvement with use of aureomycin although two myringotomies were performed. When penicillin was added after four days of aureomycin treatment, the otitis media subsided. This patient received the full 10-day course of aureomycin. A fifth child, with uncomplicated pertussis, showed improvement in the clinical picture after the first 10-day course of aureomycin. In the fourth week of disease she had a relapse with severe paroxysms, cyanosis, and attacks of apnea. Improvement followed the second course of medication in one week. A sixth patient, with pertussis and suppurative otitis media, failed to show improvement in the otitis media after 10 days of aureomycin treatment. Improvement occurred with penicillin and sulfadiazine. A seventh patient, who was treated at home with aureomycin for three days, was admitted to the hospital when bronchopneumonia developed. A nasopharyngeal culture of this patient, in the control group, showed Hemophilus influenzae, and the child improved rapidly with penicillin and sulfonamide therapy. The eighth child had pertussis and pneumonia, with Bacillus pyocyaneus (Pseudomonas aeruginosa) in the nasopharynx which was sensitive to streptomycin and resistant to aureomycin. The patient had done poorly with aureomycin treatment but on the fifth day showed a very marked improvement when streptomycin was substituted. The use of aureomycin was discontinued after one day because of marked abdominal distention in the ninth patient in the control group, who had pertussis and pneumonia. The 10th patient had severe diarrhea and vomiting on the seventh day of medication. Improvement followed the discontinuance of the medication.

## COMMENT

The course of pertussis is so variable that it is extremely difficult to compare the disease in different patients. It was our impression that improvement was always more apparent in the severely ill patients than in the mildly ill patients. In order to equalize the influence of nursing care, aureomycin and the placebo were given every four hours day and night so that the patients in each group were disturbed an equal number of times. The course of pertussis has a definite pattern, and deviations from this pattern can be demonstrated only by comparing the course of the disease in patients in the same period of the disease. For example, it is illogical to compare the course of pertussis in patients in the first week of disease with the disease in patients who came under treatment at a later period. Other factors, such as age, severity of the disease, complications, and the previous state of health, influence the pattern of pertussis. The frequency of paroxysms in itself is not a true index of the severity of the disease, especially in newborn infants and small or debilitated infants. The mean severity index as derived in this study is based upon more than one clinical sign and is therefore more representative of the symptomatology of the disease than is the number of paroxysms alone.

When improvement did occur in the aureomycin-treated patients, it was not dramatic. The greatest difference in the rate of improvement between the two groups was in patients under one year old. In general, improvement in the pertussis syndrome was gradual, although in isolated instances it appeared to be very marked. There may be this difference between the two groups because pertussis has a tendency to become severer in younger patients.

## CONCLUSIONS

There appears to be no evidence to show that aureomycin gives significantly better results in the treatment of pertussis than does supportive treatment including no antibiotics, penicillin, streptomycin, or sulfadiazine. Aureomycin is a valuable adjunct to the medicaments for the treatment of pertussis but does not appear to exert a curative effect on the disease. Along with other measures, including use of oxygen, sedation, nasopharyngeal aspirations, and proper nursing care, aureomycin may be of value in the management of the disease. The value of good nursing care cannot be overemphasized for the successful treatment of pertussis.

## SUMMARY

Eighty-five patients with pertussis were treated with 50 mg. of aureomycin per kilogram of body weight daily for 10 days, and 74 parallel controls received chemotherapy, penicillin, streptomycin, or sulfadiazine.

The difference in the course of pertussis between the aureomycin-treated patients and the control group under one year of age is slight and not statistically significant.

There was no apparent marked advantage in the course of pertussis from treatment with aureomycin over the treatment used in the control group when treatment was started after the first week of disease.

Dr. Charles B. Reiner assisted us in this study.

# STUDIES ON CYSTIC FIBROSIS OF THE PANCREAS

## Role of Various Diluents and the Dilution Factor in the Interpretation of the X-Ray-Film Test for Fecal Trypsin

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FALSELY positive tests for fecal trypsin due to bacterial gelatinase [1] were found for more than one-half of 137 children [2] with cystic fibrosis of the pancreas whose feces were tested by the x-ray-film technique.[3] Previous studies [4] have indicated that soybean trypsin inhibitor will inhibit gelatin liquefaction due to pancreatic trypsin and pancreatin-U.S.P. but not that due to bacterial gelatinase.

The reliability and consistency of results obtained by the "spot film" technique for fecal trypsin are affected by the following factors:

(1) The pH of the fecal suspension [1]
(2) Age of the specimen
(3) Consistency of the stool
(4) Differences in the type of x-ray and photographic film used in the test [5]
(5) Presence of barium and certain other heavy metal ions in high concentration in the fecal specimen [6]
(6) Temperature at which the fecal suspension is incubated on the x-ray film
(7) Presence of bacterial gelatinase [7]
(8) Length of time the fecal suspension is left on the film
(9) Rubbing [3] during the washing process after the incubation period, which may result in mechanical removal of incompletely digested gelatin film
(10) Temperature of the water used during the washing process

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Presented before the Society for Pediatric Research, Atlantic City, N. J., May 3, 1951.

From the Departments of Pediatrics, Baltimore City Hospitals and the Johns Hopkins University School of Medicine.

1. Johnstone, D. E.: Studies on the Gelatin-Liquefying Properties of Certain Bacteria, with Particular Reference to the Laboratory Diagnosis of Cystic Fibrosis of the Pancreas, Pediatrics **6**:351, 1950.

2. Johnstone, D. E., and Neter, E.: Studies on the Laboratory Diagnosis of Cystic Fibrosis of the Pancreas: Positive Gelatin Film Tests Due to Gelatin-Liquefying Bacteria in Feces and Duodenal Juice, Pediatrics **7**:483, 1951.

3. Shwachman, H.; Patterson, P. R., and Laguna, J.: Studies in Pancreatic Fibrosis: A Simple Diagnostic Gelatin Film Test for Stool Trypsin, Pediatrics **4**:222, 1949.

4. Johnstone, D. E., and Neter, E.: Differentiation Between Bacterial and Tryptic Gelatin Liquefaction as an Aid to the Diagnosis of Fibrosis of the Pancreas, Proc. Soc. Exper. Biol. & Med. **74**:326, 1950.

5. Footnotes 1 and 4. Gaffney, P. C.: Source of Error in Test for Stool Trypsin, Pediatrics **8**:82, 1951.

6. Johnstone and Neter.[4] Johnstone, D. E.: Unpublished data.

7. Johnstone.[1] Johnstone and Neter.[2]

A dilution factor may also be important. This was suggested by the data obtained by studying the proteolytic activity in dilutions of fecal specimens from children [2] with pancreatic insufficiency. The fecal trypsin studies on those children suggested that one might exclude a falsely positive test due to bacterial gelatinase, if the test specimen liquefied the gelatin coating of the x-ray film in a dilution of 1:120 or higher. It was the purpose of this study to verify the importance of the dilution factor and the use of various diluents in interpreting the results of this test. Attempts were also made to develop a new method for the quantitative determination of the trypsin content of feces and duodenal juice, using a quantitative trypsin inhibitor technique.

## METHODS

Fresh fecal specimens were obtained from children varying in age from birth to 15 years. Patients with steatorrhea, diarrhea, constipation, and liver disease were excluded. In the case of premature infants and full-term newborn infants, the first three meconium specimens passed were tested. Thereafter, approximately two specimens were examined each week until the patients left the hospital. The specimens were examined within 12 hours after collection or were kept refrigerated until studied.

One gram of feces was suspended by shaking in 5 cc. of diluent, making a 1:6 dilution. Multiple dilutions up to 1:12,288 were made with each specimen. Sterilized distilled water was used as a diluent for all but a few of the tests. Many specimens were tested simultaneously with isotonic (1.3%) and 5% sodium bicarbonate, isotonic sodium chloride solution, and barbiturate buffer (7 parts of N/10 sodium barbiturate to 3 parts of N/10 hydrochloric acid, pH 8.0).

Only Eastman Kodak "Blue Brand" x-ray film was used. One side of the film was wetted with warm water and scraped clean of its gelatin coating before use. Circles 2 cm. in diameter were made on the unscraped side with a wax pencil. The film was placed in a Petri dish, emulsion side up, and 2 drops of each dilution tested were placed in separate circles on the film. The Petri dish was covered to prevent drying and placed in an incubator at 37 C. One hour later a stream of cold water was played for approximately five seconds on the side of the film which had been in contact with the test suspension. Rubbing of the x-ray film during the washing process was purposely omitted to avoid mechanical removal of incomplete digested gelatin film. In reading a test, a positive result was recorded only if the gelatin film was completely digested so that one could see through the film distinctly when it was placed against a dark background or held up to a light.

The effect of exposure to air on the pH and gelatin-liquefying properties of 5% sodium bicarbonate were studied. Spot-film tests for gelatin liquefaction and determination of pH with a glass electrode were done on fresh 5% sodium bicarbonate solution, and again on the same solution after exposure to air at room temperature after 5, 24, 48, 72, and 96 hours.

To determine the frequency of gelatinase-producing bacteria in normal feces, a tube of sterile nutrient gelatin broth was inoculated with a loopful of each specimen and incubated for 24 hours. A loopful from this first tube was subcultured on two successive days on the same media. If the third tube failed to gel upon refrigeration, a loopful of this material was then streaked out on various solid culture media for isolation and identification of the gelatin-liquefying bacteria.

In an effort to make quantitative determinations of the trypsin content of a suspension, a titration method, using soybean trypsin inhibitor was set up. This inhibitor occurs in large quantities in navy beans and soybeans [8] and is responsible for the excessive fecal protein loss when unheated soybean meal is fed to infants or to experimental animals. To determine the amount of this heat-labile trypsin inhibitor required to prevent gelatin liquefaction by a known amount of trypsin, eight trypsin-soybean-trypsin-inhibitor titrations were done by the following

8. Boman, D. E.: Fractions Derived from Soy Beans and Navy Beans Which Retard Digestion of Casein, Proc. Soc. Exper. Biol. & Med. **57**:139, 1944. Kunitz, M.: Crystallization of Trypsin Inhibitor from Soy Bean, Science **101**:668, 1945.

method. Standard solutions of trypsin and soybean trypsin inhibitor were prepared from accurately weighed amounts of the two crystalline substances.[9] These were used to make dilutions ranging from 0.001 to 10.0 mg. per cubic centimeter. The trypsin dilutions were prepared just prior to testing and were kept packed in crushed ice until used. Two-tenths cubic centimeter of each dilution and soybean trypsin inhibitor was mixed with an equal volume of each dilution of crystalline trypsin in 5 cc. tubes. The tubes were shaken, and the mixtures were deposited in individual wax-penciled circles on the x-ray film. The test for gelatin liquefaction was then run and interpreted precisely as the tests on feces. The end-point of each dilution mixture was taken as that amount of soybean trypsin inhibitor required to prevent complete liquefaction of the x-ray film. In an attempt to adapt this technique to quantitative stool-trypsin analysis, equal quantities of each fecal dilution tested were mixed in similar tubes with varying dilutions of soybean trypsin inhibitor. In each instance the results were recorded so as to indicate the milligrams of soybean trypsin inhibitor required to inhibit the activity of 1 gm. of feces.

TABLE 1.—*Results of Roentgenographic-Film Tests for Trypsin on Feces of Normal Children, Arranged According to Age*

| Classification of Infants | Specimens, No. | Patients, No. | Positive Fecal X-Ray Film Tests in 1:96 Dilution or Higher | | | | Data of Shwachman and Colleagues,* Positive Tests in 1:10 Dilution | |
|---|---|---|---|---|---|---|---|---|
| | | | Meconium | | Subsequent Stools | | | |
| | | | Number† | Per Cent | Number† | Per Cent | Number† | Per Cent |
| Premature | | | | | | | | |
| Group I (less than 1,000 gm.) | 56 | 12 | 19/22 | 86 | 29/34 | 85 | †..... | .. |
| Group II (1,000-1,499 gm.) | 115 | 15 | 60/69 | 87 | 46/46 | 100 | ..... | .. |
| Group III (1,500-1,999 gm.) | 283 | 28 | 84/114 | 74 | 169/170 | 99 | ..... | .. |
| Group IV (2,000-2,499 gm.) | 139 | 23 | 48/73 | 66 | 66/66 | 100 | ..... | .. |
| Total | 593 | 78 | 211/278 | 76 | 310/316 | 98 | 28/28 | 100 |
| Full-term newborn | 153 | 39 | 61/80 | 76 | 75/78 | 96 | ..... | .. |
| Under 2 yr. | 91 | 46 | ..... | .. | 89/91 | 98 | 223/233 | 96 |
| 2-5 yr. | 17 | 12 | ..... | .. | 16/17 | 94 | 117/133 | 88 |
| 5-10 yr. | 59 | 27 | ..... | .. | 50/59 | 85 | 40/74 | 54 |
| 10-15 yr. | 33 | 14 | ..... | .. | 31/33 | 91 | 8/32 | 25 |
| Totals | 946 | 216 | 272/358 | 76 | 571/594 | 96 | 416/500 | 83 |

* "Stool Trypsin in Normal and Sick Individuals Exclusive of Pancreatic Fibrosis, Arranged According to Age." [8]
† In each fraction the denominator indicates the number of tests done, the numerator the number of positive reactions.

## RESULTS

Table 1 shows the age distribution of the patients studied and the percentage of fecal specimens giving positive x-ray-film tests for tryptic activity. In the case of newborn full-term and premature infants, the results are divided into those done on meconium and those done on subsequent stools. The data of Shwachman and his colleagues [3] on children of similar age groups are also shown for comparison. Approximately 76% of the meconium specimens in our series gave a positive test in a dilution of 1:96 or greater. All were positive in a 1:6 dilution. Tests on subsequent fecal specimens were positive in 98% of the premature infants and in 96% of the full-term newborn infants. In Charts 1 and 2 the results are listed graphically according to the highest dilution giving a positive test. As may be seen from Chart 1, the specimens of some of the smallest premature infants gave positive tests in a dilution up to 1:6, 144 on the first day of life.

From Charts 1 and 2 it can be calculated that in the present series 92% of postmeconium specimens in children up to the age of 5 years gave positive reactions

9. Both crystalline trypsin and soybean trypsin inhibitor may be purchased from the Worthington Biochemical Laboratory, Freehold, N. J.

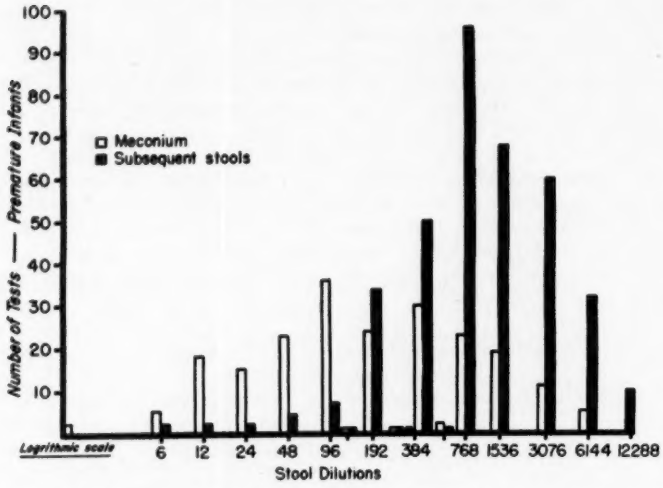


Chart 1.—The highest fecal dilution of each specimen giving a positive test for gelatin liquefaction; frequency of occurrence in 78 patients.

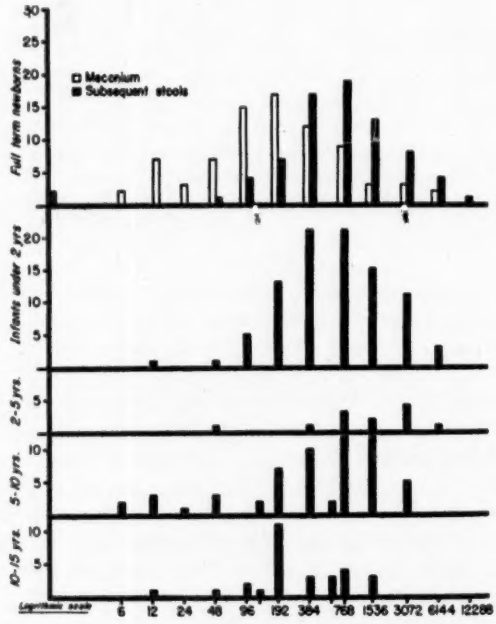


Chart 2.—Specimens of each age group arranged according to the highest stool dilution capable of completely digesting the gelatin film.

in a dilution of 1:192 or higher. Eighty per cent were positive in a dilution of 1:384 or higher. It may have been that the meconium specimens as well as many of the subsequent specimens of all age groups which failed to liquefy gelatin in a dilution of 1:96 would have done so had they been suspended in barbiturate buffer solution instead of in distilled water.

In Table 2 are shown the results of testing specimens from children of all ages, with four different diluents being used. Of the three premature infants listed in

TABLE 2.—*Influence of Different Diluents on Gelatin-Liquefying Capacity of Fecal Suspensions*

| Classification of Infants | Patient | Diluents: Distilled Water, Dilution* | Barbiturate Buffer, pH 8.0,† Dilution | 1.3% Sodium Bicarbonate (Isotonic), Dilution | 5% Sodium Bicarbonate, Dilution |
|---|---|---|---|---|---|
| Premature (meconium) ..... | G. I. | 1:96 | 1:3,072 | 1:3,072 | 1:3,072 |
| | B. T. | 1:384 | 1:3,072 | 1:3,072 | 1:3,072 |
| | J. E. | 1:96 | 1:384 | ..... | ..... |
| Under 2 yr. ..... | T. P. | 1:384 | 1:3,072 | 1:3,072 | 1:3,072 |
| | G. H. | 1:192 | 1:768 | ..... | ..... |
| 2-5 yr. ..... | D. W. | 1:96 | 1:384 | 1:768 | 1:768 |
| 5-10 yr. ..... | J. B. | 1:24 | 1:120 | 1:1,536 | 1:3,072 |
| | D. H. | 1:48 | 1:192 | 1:192 | 1:768 |
| Over 10 yr. ..... | E. D. | 1:96 | 1:384 | 1:384 | 1:384 |
| Infants with cystic fibrosis of the pancreas ..... | M. C. | 1:6 | 1:12 | 1:24 | 1:192 |
| | M. F. | 1:6 | 1:6 | 1:96 | 1:768 |
| | G. W. | 1:48‡ | 1:48 | 1:384 | 1:384 |

* The highest dilution of the fecal suspension giving a positive gelatin-liquefaction reaction on the x-ray film.
† Seven parts of N/10 sodium barbiturate to three parts of N/10 hydrochloric acid.
‡ This patient's feces contained bacterial gelatinase.

TABLE 3.—*Influence of Prolonged Exposure to Air on the pH and Gelatin-Liquefying Capacity of Various Diluents*

| Time After Preparation of Solution, Hr. | 5% $NaHCO_3$: Solution 1 pH | Solution 1 Gel-Liq.* | Solution 2 pH | Solution 2 Gel-Liq.* | Solution 3 pH | Solution 3 Gel-Liq.* | Distilled Water: Solution 1 pH | Solution 1 Gel-Liq.* | Solution 2 pH | Solution 2 Gel-Liq.* | Barbiturate Buffer pH | Barbiturate Buffer Gel-Liq.* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Under 1..... | 7.60 | 0 | 8.28 | ±† | .... | ..... | 5.00 | 0 | 6.00 | 0 | 8.0 | 0 |
| 5..... | 8.20 | 0 | 8.36 | + | .... | ..... | 6.40 | 0 | .... | ..... | .... | ..... |
| 24..... | 8.60 | ++ | 8.62 | ++ | 8.72 | + | 6.42 | 0 | .... | ..... | .... | ..... |
| 48..... | 9.30 | +++ | 8.83 | +++ | 8.96 | +++ | .... | ..... | .... | ..... | .... | ..... |
| 72..... | ? | ++++ | 8.92 | +++ | 9.10 | ++++ | .... | ..... | .... | ..... | .... | ..... |
| 96..... | .... | ..... | 9.08 | +++ | .... | ..... | .... | ..... | .... | ..... | .... | ..... |
| 120..... | .... | ..... | 9.19 | ++++ | .... | ..... | 6.62 | 0 | 6.65 | 0 | 8.0 | 0 |

* Liquefaction of the gelatin coating on x-ray film; tests performed as for fecal trypsin.
† In this analysis 1+ signifies partial digestion of the gelatin film; 4+ signifies complete digestion.

Table 2, meconium specimens from two failed to liquefy the gelatin in a dilution of 1:120 or higher when the specimens were suspended in distilled water. However, when the barbiturate buffer solution was used, all three gave positive tests in high dilutions.

It is important to realize that 5% sodium bicarbonate, which is used as a stool diluent in some hospitals, may itself be gelatin-liquefying. In Table 3 are listed the changes in pH and gelatin-liquefying capacity of 5% sodium bicarbonate, distilled water, and barbiturate buffer, which occur after exposure to room air for various

time intervals. The longer the solution of 5% sodium bicarbonate is exposed to room air, the higher is its pH and gelatin-liquefying capacity.

Table 4 shows the results of stool cultures on 195 of the 216 normal patients listed in Table 1. Twenty-eight per cent of patients had gelatin-liquefying bacteria

TABLE 4.—*Incidence of Gelatin-Liquefying Bacteria in Feces on Normal Children Studied*

| Classification of Infants | Stools with Gelatin-Liquefying Bacteria * | | Patients with Gelatin-Liquefying Bacteria in Feces | | Strains of Gelatin-Liquefying Bacteria Encountered, No. | | |
|---|---|---|---|---|---|---|---|
| | No. | Per Cent | No. | Per Cent | Pseudomonas Aeruginosa | Proteus (Untyped) | Unidentified |
| Premature | | | | | | | |
| Group I | 2/53 | 3 | 1/12 | 8 | .. | .. | .. |
| Group II | 14/76 | 18 | 6/15 | 40 | .. | .. | .. |
| Group III | 36/221 | 16 | 10/28 | 36 | .. | .. | .. |
| Group IV | 41/91 | 45 | 9/21 | 43 | .. | .. | .. |
| Total | 93/441 | 21 | 26/76 | 34 | 16* | 4 | 1 |
| Full-term newborn | 6/83 | 7 | 4/39 | 10 | 1 | .. | 3 |
| Under 2 yr. | 23/66 | 37 | 15/45 | 33 | 10* | 2 | 4 |
| 5-10 yr. | 7/25 | 28 | 5/22 | 23 | 2 | 1 | 2 |
| 10-15 yr. | 8/16 | 50 | 5/13 | 38 | 2 | 1 | 2 |
| Totals | 137/631 | 22 | 55/195 | 28 | 31 | 8 | 18 |

* Some patients harbored two strains of gelatin-liquefying bacteria.

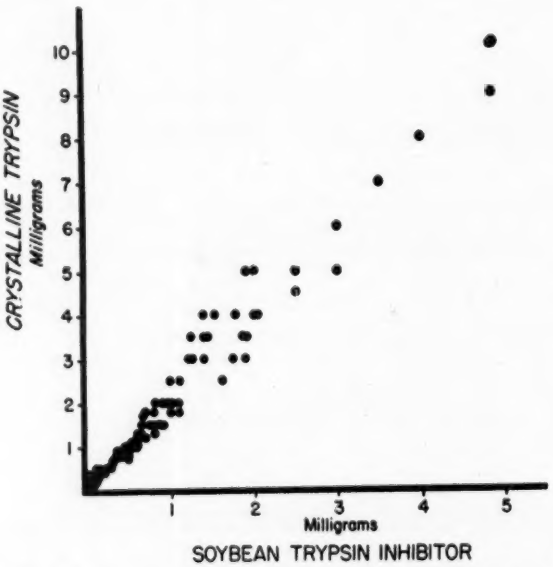


Chart 3.—Minimum amount of soybean trypsin inhibitor required to inhibit gelatin liquefaction by varying amounts of crystalline trypsin; represented by dots.

in the feces at some time. Pseudomonas aeruginosa was the most frequently encountered organism. Few strains isolated, however, possessed as great gelatin-liquefying capacity as strains recovered in previous studies.[1]

Chart 3 shows the results of experiments done to determine the amount of soybean trypsin inhibitor required to inhibit liquefaction of x-ray-film gelatin by vary-

ing amounts of trypsin. The data suggest that 1 mg. of soybean trypsin inhibitor inhibits approximately 2 mg. of crystalline trypsin. A similar titration technique substituting various dilutions of fecal and duodenal juice for the crystalline trypsin was attempted. However, it failed to give reproducible results. Soybean trypsin inhibitor was found to be useful, nonetheless, for qualitative identification of trypsin and its differentiation from gelatin-liquefying bacterial gelatinase in feces and duodenal juice.

## COMMENT

Since the first figures on stool trypsin in normal and sick persons as tested by the x-ray-film test were published,[3] many persons have been under the impression that this technique for the detection of fecal trypsin is of little value, particularly for children in the older age groups. The data of this study suggest that in infants under 2 years old, the group in which manifestations of cystic fibrosis of the pancreas are most likely to occur, 98% of normal subjects will have a positive test for fecal trypsin in a stool dilution of 1:96 or higher when the specimen is suspended in distilled water. The percentages may be even higher if barbiturate buffer solution is used as a diluent. Unlike sodium bicarbonate solutions, barbiturate buffer and distilled water are stable for indefinite periods, unless accidentally contaminated with bacterial gelatinase.

The data on premature infants are of interest in view of the recent work of Werner,[10] Magnusson,[11] and Jorpes[12] which suggested that prematurely born infants have an immature and inferior protein-splitting capacity of the intestinal tract. The present data indicate the presence of trypsin in the intestinal tract and support the work of Madey and Dancis[13] and others[14] who showed that premature infants can handle protein efficiently. The first meconium specimen of the smallest premature infant in this study (birth weight 634 gm.) gave a positive test for fecal trypsin in a 1:384 dilution.

In a previous study[2] it was found that although 60% of 137 children with pancreatic deficiency had a falsely positive test for fecal trypsin, no specimen gave a positive reaction in a dilution greater than 1:120. The data from this study suggest that of the fecal samples of children under 2 years old, 98% will liquefy the gelatin coating of x-ray-film in a dilution of 1:96 or higher. Consequently, one would expect that dilution of a sample to be tested to at least 1:120 should eliminate or drastically reduce the possibility of a falsely positive test due to bacterial gelatinase. To insure accurate preparation of the original 1:6 fecal suspension, the specimens must be weighed. Subjective estimation of the size of the sample is inaccurate, since the specific gravity of fecal specimens varies with its fat and water content.

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None of the gelatin-liquefying organisms found in the feces of the normal children in this series was found capable of liquefying gelatin in a dilution of 1:50 when x-ray-film tests were done on varying dilutions of 24-hour pure-broth cultures.

In performing this test routinely on the feces of patients suspected of having cystic fibrosis of the pancreas, it is recommended that the initial fecal suspension (1:6, as described above under "Method") be diluted tenfold (1:60), twentyfold (1:120) and thirtyfold (1:180). X-ray-film tests should be done on these four dilutions and on the diluent as a control.

If a test for fecal trypsin, performed as herein described on a fresh soft specimen, is persistently negative in all dilutions, the patient may be considered to have no trypsin in the feces. If the test is repeatedly positive but always in a dilution of less than 1:120, the explanation may be (1) that the patient has cystic fibrosis of the pancreas with a falsely positive test due either to bacterial gelatinase or to ingested pancreatin, or (2) that he has "incomplete" [15] or "partial" [16] cystic fibrosis of the pancreas. However, absolute proof that such an incomplete or partial stage of the disease exists is still lacking.

One may identify the presence of gelatinase-producing bacteria by the nutrient-gelatin-broth-inoculation technique (as described above under "Method"). When one is uncertain whether gelatin liquefaction of the x-ray-film by feces or duodenal juice is due to pancreatogenic trypsin or ingested pancreatin rather than to gelatinase, the matter can be settled by the use of soybean trypsin inhibitor. If equal amounts of a 1:60 dilution of a normal stool (capable of liquefying gelatin in a dilution of 1:120) and a solution of soybean trypsin inhibitor containing 2 mg. per cubic centimeter are mixed in a test tube and the mixture tested for its gelatin-liquefying capacity by the x-ray-film technique, the liquefaction should be prevented. If the liquefaction had been due to bacterial gelatinase alone, the addition of soybean trypsin inhibitor would not inhibit the liquefaction.

## SUMMARY AND CONCLUSIONS

By the x-ray-film technique 9,600 tests for fecal trypsin were performed on 963 specimens from 216 children without known intestinal disease. Of postmeconium specimens so tested 96% gave positive results in a dilution of 1:96 or higher. In children under 5 years old 92% of the specimens gave positive tests in a dilution of 1:192 or higher. One-third of the specimens harbored gelatin-liquefying bacteria. The importance of different diluents as a source of error is discussed.

Recommended modifications in the x-ray-film test for fecal trypsin are presented. Although a method for quantitative determination of the amount of crystalline trypsin present in pure solution is possible using a soybean-trypsin-inhibitor technique, a similar method using dilutions of fecal suspensions instead of crystalline trypsin was not successful.

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The helpful suggestions of Dr. Harold E. Harrison and Dr. Francis F. Schwentker during the study and preparation of the manuscript are acknowledged.

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# SEASONAL INCIDENCE OF PATENT DUCTUS ARTERIOSUS AND MATERNAL RUBELLA

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GREGG'S report [1] in 1941 stimulated interest in the etiological relationship of environmental factors in early pregnancy to congenital defects in the child. His observations relating maternal rubella to congenital cataract and congenital heart disease were supported by the more extensive study of Swan and his associates,[2] which also revealed that deaf-mutism and microcephaly were related to maternal rubella. Later Evans [3] reported delayed eruption of teeth as another manifestation of the rubella syndrome.

The frequent implication that patent ductus arteriosus and septal defects are related to maternal rubella [4] is not supported by any conclusive data in existing literature. Among 442 reported cases of congenital heart disease following maternal rubella,[5] it was possible to find only 77 in which a specific heart lesion was noted.[6]

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*(Footnotes continued on next page)*

The specific lesions reported[7] were as follows: 42 patent ductus arteriosus, of which 17 were specified as "probable"; 36 septal defects, of which 28 were specified as "probable" or "possible"; 1 tetralogy of Fallot; 1 coarctation of aorta; 3 patent foramen ovale; and 1 "patent foramen ovale in the interventricular septum."

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*(Footnotes continued on next page)*

A study of records at the Children's Hospital in Boston was undertaken in an attempt to define more precisely the relationship of environmental factors to subsequent congenital cardiac anomalies in children. Specific information concerning maternal infection early in pregnancy was lacking or incomplete in many of these records, thus making an extensive correlative study impossible. It was believed, however, that useful information concerning this relationship could be obtained by a correlation of specific congenital cardiac diagnoses with one reliable datum in the records, namely, the birth date of the child. This approach is based on the following premises: 1. If children have specific congenital heart anomalies which are associated with genetic or other nonseasonal factors,[8] their birth dates tabulated by months would be similar in distribution to the birth dates of all children born during the same period in the same area. 2. If seasonal environmental factors were operative in producing certain congenital anomalies, the birth dates of infants with such congenital anomalies would have a seasonal distribution.

## METHODS AND RESULTS

A study was made at the Children's Hospital of all records of children born during the period from Jan. 1, 1934, through Dec. 31, 1948, for whom a definite diagnosis of congenital heart disease was made during the period Jan. 1, 1934, through March 15, 1949. The period for diagnosis in the study was extended beyond Dec. 31, 1948, to permit at least a short period of observation for those born late in 1948. The opportunity for recognizing congenital heart disease was greater for children born early than for those born late in the study period, since the longer the period of observation after birth the more likely is the recognition of the disease.

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7. Multiple lesions were diagnosed in several cases.

8. In this study it is assumed that genetic factors are nonseasonal.

In this study the term congenital heart disease is defined to include primary lesions of the heart, primary lesions of vessels communicating directly with the heart, and persistence of the ductus arteriosus. The ductus arteriosus is, however, included only when it is patent for at least six months after birth,[9] since prior to that time the ductus may be normally patent or its small size may make diagnosis doubtful. All cases, without selection, in which there were any of the diagnoses listed in Table 1 were included in the study.

TABLE 1.—*Cardiac Anomalies Included in the Study, Children's Hospital, Jan. 1, 1934-Dec. 31, 1948*

- Aortic (thoracic) anomalies
  - Aneurysm of ascending aorta
  - Coaretation
  - Dextroaorta (overriding)
  - Double aortic arch
  - Right aortic arch
  - Underdevelopment
- Anomalies of chambers of the heart
  - Cor biloculare
  - Cor triloculare
  - Left auricle
    - Aplastic
    - Double
    - Hypoplasia
  - Left ventricle
    - Accessory ventricle within left ventricle
    - Hypoplasia
    - Small
  - Right ventricle
    - Accessory
    - Hypoplasia
- Patent ductus arteriosus (if patent 6 months after birth)
- Septal defects
  - Auricular
  - Ventricular
- Tetralogy of Fallot
- Transposition of great vessels
- Valvular anomalies
  - Aortic
    - Absence
    - Anomaly of leaflets
    - Atresia
    - Stenosis
  - Mitral
    - Absence
    - Anomaly of leaflets
    - Hypoplasia
  - Pulmonary
    - Absence
    - Anomaly of leaflets
    - Atresia
    - Stenosis
  - Tricuspid
    - Anomaly of leaflets
    - Atresia
    - Hypoplasia
    - Stenosis
  - Tricuspid and mitral
    - Common atrioventricular valve
    - Transposition of atrioventricular valves
- Miscellaneous anomalies
  - Anomalous chordae tendineae
  - Anomalous coronary artery
  - Anomalous venous return to the heart
  - Aortic septal defect
  - Communication between the left auricle and the pulmonary artery
  - Dextrocardia
  - Dextroversion
  - Eisenmenger complex
  - Fetal endomyocarditis
  - Herniation of cusp of aortic valve and sinus of Valsalva into the right ventricle
  - Lutembacher syndrome
  - Octology of Emergreen
  - Pulmonary artery
    - Absence
    - Anomalous
    - Atresia
    - Hyperplasia
    - Hypoplasia
    - Stenosis
  - Pulmonary conus
    - Dilatation
    - Stenosis
  - Subaortic stenosis
  - Telangiectasia of myocardium
  - Truncus arteriosus
- "Congenital heart" (unspecified cardiac anomaly)

The study includes 1,042 cases in which a diagnosis of congenital heart disease was made and was verified by one of the authors (F. P. H.) on the basis of autopsy findings or surgical or clinical evidence. The 257 diagnoses based upon autopsy findings and the 260 diagnoses based on surgical evidence were accepted without question. The 525 diagnoses based on clinical evidence were appraised by strict reevaluation of the patient's history, physical examination, and laboratory data. A definitive diagnosis of a specific lesion was made on the basis of the clinical findings in 191 of the 525 cases. In the remaining 334 cases the clinical evidence permitted a definitive diagnosis of congenital heart disease but not a conclusive differential diagnosis, and these were therefore classified as "congenital heart."

9. The one exception to this is G. T., in whom patent ductus arteriosus required surgical intervention at the age of 2 months.

The distribution of live births in Massachusetts for the years 1934 through 1948 was used for comparison with the births of the children in the study.[10] Live births in Massachusetts[11] by month of birth, from the Annual Reports on Vital Statistics in Massachusetts for the years 1934-1948, are distributed more or less evenly throughout the year, except for a slight seasonal increase in the months of June through October (Table 2). When these data are analyzed according to births per day by months to correct for the variation among lengths of months, this slight seasonal increase persists. Birth dates of the 1,042 children in the study were tabulated by actual month of birth[12] and specific heart diagnosis in two ways: (1) by patients (Table 3) and (2) by specific lesions (Table 4), multiple heart lesions being present in certain cases.

Table 3 shows distribution of individual children with single and multiple diagnoses and with unspecified "congenital heart" diagnosis. Birth dates of all children with congenital heart disease in Table 3 have a seasonal pattern which

TABLE 2.—*Live Births in Massachusetts, Jan. 1, 1934-Dec. 31, 1948**

| | Births | | | |
|---|---|---|---|---|
| | Totals by Months | | Average per Day by Months † | |
| Months | Number | Per Cent | Number | Per Cent |
| Jan. | 92,221 | 8.12 | 2,974.9 | 7.98 |
| Feb. | 86,816 | 7.65 | 3,073.1 | 8.24 |
| March | 96,763 | 8.52 | 3,121.4 | 8.37 |
| April | 92,011 | 8.10 | 3,067.0 | 8.22 |
| May | 95,369 | 8.40 | 3,076.4 | 8.25 |
| June | 94,817 | 8.35 | 3,160.6 | 8.47 |
| July | 100,149 | 8.82 | 3,230.6 | 8.66 |
| Aug. | 99,218 | 8.74 | 3,200.6 | 8.58 |
| Sept. | 96,586 | 8.51 | 3,219.5 | 8.63 |
| Oct. | 97,001 | 8.54 | 3,129.1 | 8.39 |
| Nov. | 91,057 | 8.02 | 3,035.2 | 8.14 |
| Dec. | 93,420 | 8.23 | 3,013.5 | 8.08 |
| Total | 1,135,428 | 100.00 | 37,301.9 | 100.01 |

* Figures obtained from data in Annual Reports on Vital Statistics in Massachusetts, 1934-1948.
† Data corrected for the variation among lengths of months.

differs significantly from that of all live births in Massachusetts (Table 2). Births are greater than expected in the months of April and May and in the four months, October, November, December, and January. This seasonal distribution of all cases with congenital heart disease might be the result of a similar seasonal pattern in one or another of the constituent specific anomalies.

There were adequate numbers of cases for analysis[13] of only four single cardiac defects: patent ductus arteriosus, septal defect, tetralogy of Fallot, and coarctation

10. Seasonal variations in the distributions of birth dates of children with specific heart lesions were compared with the per cent distribution of live births in Massachusetts, using the $\chi^2$ test for significance, with $P < .05$ used as the level of significance.

11. Allocated to place of residence of the parents.

12. In the beginning of the study the expected month of birth was used, since a variation in lengths of gestation might significantly affect the monthly distribution of births. A $\chi^2$ test did not indicate a significant difference between actual and expected months of births of the total group. Actual birth dates, being the more reliable, were therefore used in all tabulations.

13. A total frequency of at least 40 was selected as the minimum requirement for the validity of the $\chi^2$ test.

of aorta. These are tabulated separately in Table 3. Of these four anomalies, only patent ductus arteriosus has a significant seasonal distribution ($P < .01$) in which the number of cases in the season of October through January is greater than expected. The slight increase in occurrence of septal defects in the months of

TABLE 3.—*Distribution of Children with Congenital Heart Disease by Diagnosis and Month of Birth, Children's Hospital, Jan. 1, 1934-Dec. 31, 1948*

| | Single Cardiac Anomalies | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Month of Birth | Patent Ductus Arteriosus | Septal Defect | Tetralogy of Fallot | Coarctation of Aorta | Other * | Multiple Cardiac Anomalies | "Congenital Heart" † | Total |
| Jan | 25 | 7 | 8 | 8 | 12 | 12 | 23 | 90 |
| Feb | 12 | 10 | 4 | 8 | 5 | 10 | 20 | 69 |
| March | 12 | 7 | 3 | 4 | 5 | 15 | 29 | 75 |
| April | 17 | 8 | 6 | 6 | 11 | 13 | 33 | 94 |
| May | 19 | 6 | 4 | 4 | 13 | 14 | 36 | 96 |
| June | 14 | 7 | 2 | 1 | 7 | 18 | 21 | 70 |
| July | 9 | 4 | 11 | 7 | 5 | 10 | 30 | 76 |
| Aug | 15 | 12 | 6 | 4 | 13 | 18 | 22 | 90 |
| Sept | 20 | 9 | 4 | 2 | 10 | 13 | 25 | 83 |
| Oct | 29 | 9 | 3 | 4 | 9 | 24 | 27 | 105 |
| Nov | 24 | 10 | 10 | 3 | 4 | 18 | 37 | 106 |
| Dec | 25 | 9 | 2 | 1 | 3 | 17 | 31 | 88 |
| Total | 221 | 98 | 63 | 47 | 97 | 182 | 334 | 1,042 |

* Anomalous coronary arteries, anomalous venous return to the heart, aortic anomalies other than coarctation, dextrocardia, Eisenmenger complex, fetal endomyocarditis, Lutembacher syndrome, shortening of chordae tendineae, telangiectasia of myocardium, transposition of great vessels, truncus arteriosus, valvular anomalies.
† Unspecified cardiac anomaly.

TABLE 4.—*Distribution of Specific Lesions in Children by Month of Birth, Children's Hospital, Jan. 1, 1934-Dec. 31, 1948**

| Month of Birth | Patent Ductus Arteriosus | Septal Defect | Tetralogy of Fallot | Coarctation of Aorta | Miscellaneous † | "Congenital Heart" ‡ |
|---|---|---|---|---|---|---|
| Jan | 28 | 14 | 10 | 5 | 28 | 23 |
| Feb | 13 | 17 | 4 | 8 | 30 | 21 |
| March | 16 | 18 | 4 | 9 | 28 | 30 |
| April | 19 | 12 | 9 | 9 | 34 | 34 |
| May | 20 | 11 | 5 | 8 | 43 | 36 |
| June | 17 | 18 | 3 | 2 | 52 | 22 |
| July | 10 | 10 | 11 | 8 | 20 | 30 |
| Aug | 17 | 28 | 7 | 6 | 46 | 22 |
| Sept | 21 | 17 | 6 | 6 | 31 | 26 |
| Oct | 33 | 20 | 5 | 7 | 58 | 28 |
| Nov | 28 | 16 | 14 | 4 | 47 | 38 |
| Dec | 32 | 18 | 4 | 5 | 27 | 31 |
| Total | 254 | 199 | 82 | 77 | 444 | 341 |

* Each lesion is tabulated separately, irrespective of the coexistence of another cardiac anomaly in the same child.
† Anomalous chambers of the heart, anomalous coronary arteries, anomalous venous return to the heart, aortic anomalies other than coarctation, dextrocardia, dextroversion, Eisenmenger complex, fetal endomyocarditis, Lutembacher syndrome, pulmonary artery anomalies, octology of Emergreen, shortening of chordae tendineae, telangiectasia of myocardium, transposition of great vessels, truncus arteriosus, valvular anomalies.
‡ Unspecified cardiac anomaly.

August through December is not significant, and the birth-date distributions of cases of tetralogy of Fallot and of coarctation of aorta do not differ significantly from that of all live births in Massachusetts.

A study was also made of the distribution of birth dates of all children with each of the single defects, irrespective of the coexistence of another cardiac anomaly

in the same child (Table 4).[14] Each of the specific lesions present in the cases studied was tabulated by the month of birth of the child in whom the defect occurred. Only those specific lesions with a frequency large enough for significance tests [13] were tabulated separately; all others were included in the miscellaneous group. The monthly variations of the individual diagnoses of patent ductus arteriosus, septal defect, tetralogy of Fallot, and coarctation of aorta follow approximately the same pattern as the cases in Table 3. There is still apparent the slight and statistically insignificant seasonal increase in the occurrence of septal defects in August through December. In addition, there is a slight and statistically insignificant seasonal increase in coarctation of the aorta in February through May. The distribution of birth dates of cases of tetralogy of Fallot also does not differ significantly from that of all live births in Massachusetts. Only patent ductus

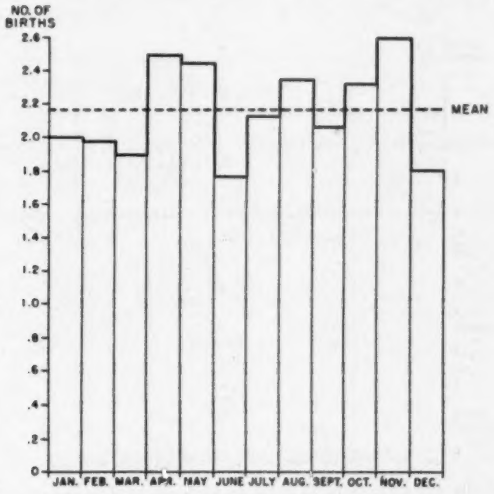


Chart 1.—Births per day by months of children with congenital heart disease other than patent ductus arteriosus, Children's Hospital, Jan. 1, 1934, to Dec. 31, 1948.

arteriosus has a significantly high seasonal incidence in the season of October through January ($P<.01$).

Chart 1 [15] shows the relatively even monthly distribution of the 788 children with congenital heart disease who do not have a diagnosis of patent ductus arteriosus.[16] In striking contrast in Chart 2,[15] the 254 cases of patent ductus arterio-

14. The total number of "congenital hearts" tabulated in Table 4 is larger than that in Table 3, since several children with multiple heart lesions consisting of a specific vessel anomaly or dextrocardia plus an unspecified heart lesion were classified under "multiple anomalies" in Table 3.

15. Charts 1 and 2 are based upon "births per day by months" instead of upon "births by months," to compensate for the variation among lengths of months.

16. One might question the inclusion of children with unspecified heart lesions, classified as "congenital heart," in this group, since some of these unspecified lesions might be patent ductus arteriosus. Since there is no significant difference between the monthly distribution of specific and nonspecific diagnoses within this group of 788 children, the inclusion of the "congenital heart" cases does not alter the monthly pattern of distribution.

sus are distributed throughout the year but with a high incidence in the season of October through January, 47.6% of the cases occurring in these four months. The presence of a significant seasonal pattern of birth dates of only those children who have a patent ductus arteriosus suggests that this distribution is probably responsible for the same seasonal pattern in the distribution of the birth dates of all 1,042 children with congenital heart disease.

Because of the implications in the literature that maternal rubella is related to congenital heart disease, an analysis was made of the records in which the presence (positive history) or absence (negative history) of maternal rubella during pregnancy was clearly stated. There was a positive history of rubella in 25 (2.4%) cases, and a negative history of rubella in 60 (5.8%) cases. In addition it was noted that there was a positive history of infectious disease, rash, or virus in 2 (0.2%) cases and a negative history of infectious disease, rash, or virus in 109 (10.5%) cases.

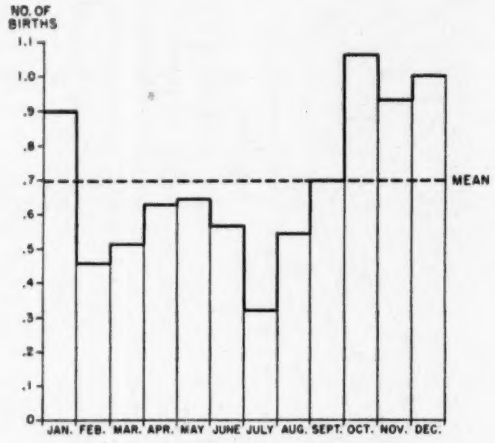


Chart 2.—Births per day by months of children with patent ductus arteriosus, Children's Hospital, Jan. 1, 1934, to Dec. 31, 1948.

Since patent ductus arteriosus was the only one of the anomalies studied which exhibited a seasonal pattern, it was of particular interest to analyze the data in regard to history of maternal rubella and presence of patent ductus arteriosus (Table 5[17]). Patent ductus arteriosus was present in 68.0% of the cases with a positive history of rubella and was absent in only 4.0% of such cases.[18] In contrast to this, patent ductus arteriosus occurred at the same low rate among those with a negative history of rubella (18.3%), with a negative history of infectious disease (20.2%) or with history unknown (24.1%).[19] The over-all differences among these

17. Since there are only two cases with a positive history of infectious disease (scarlet fever) other than rubella, they are classified with the group with history "unknown."

18. In 28.0% of this group it is not known whether the ductus arteriosus was patent.

19. One might speculate as to whether the question concerning rubella or infectious disease during pregnancy was asked most often in a selected group of cases in which there was patent ductus arteriosus. If it were, one might expect the proportion of patent ductus arteriosus among cases in which the history was unknown to be smaller than it is.

proportions are statistically significant ($P < .01$) and suggest that patent ductus arteriosus is related to rubella in this series of cases. In the 85 records in which presence or absence of rubella was clearly stated, the high proportion of patent ductus

TABLE 5.—*History of Maternal Rubella in Children with Congenital Heart Disease, Children's Hospital, Jan. 1, 1934-Dec. 31, 1948*

| | Total Cases, No. | Patent Ductus Arteriosus Present | | Patent Ductus Arteriosus Absent | | Patent Ductus Arteriosus Unknown † | |
|---|---|---|---|---|---|---|---|
| | | No. | Per Cent | No. | Per Cent | No. | Per Cent |
| Positive history of rubella.... | 25 | 17 | 68.0 | 1 | 4.0 | 7 | 28.0 |
| Negative history of rubella... | 60 | 11 | 18.3 | 27 | 45.0 | 22 | 36.7 |
| Negative history of virus, rash, or infectious disease..... | 109 | 22 | 20.2 | 49 | 45.0 | 38 | 34.9 |
| Unknown ..... | 848 ‡ | 204 | 24.1 | 370 | 43.6 | 274 ‡ | 32.3 |
| Total..... | 1,042 | 254 | 24.4 | 447 | 42.9 | 341 | 32.7 |

$\chi^2 = 30.926$; $P < .01$.

† "Congenital heart" diagnosis.
‡ Includes 2 cases with positive history of scarlet fever.

TABLE 6.—*Children with Congenital Heart Disease and a History of Maternal Rubella, Children's Hospital, Jan. 1, 1934-Dec. 31, 1948*

| Patient | Birth Date | Congenital Cardiac Anomalies | Other Congenital Anomalies |
|---|---|---|---|
| G. D..... | 1/13/36 | "Congenital heart" * | Cataract, left; deafness |
| F. B..... | 1/23/36 | "Congenital heart" * | Deafness; mental retardation |
| A. S..... | 12/ 5/41 | Patent ductus arteriosus † | Deafness |
| M. C..... | 1/10/42 | Patent ductus arteriosus † | Cataract, bilateral |
| T. C..... | 9/20/42 | Patent ductus arteriosus † | None |
| K. Z..... | 10/27/42 | Patent ductus arteriosus † | Cataract, bilateral |
| L. W..... | 10/29/42 | Patent ductus arteriosus †; pulmonary stenosis | None |
| N. S..... | 12/27/42 | Patent ductus arteriosus † | None |
| A. K..... | 1/ 9/43 | Patent ductus arteriosus †; anomalous venous return to heart | None |
| P. S..... | 2/22/43 | Patent ductus arteriosus † | Cataract, right; harelip; cleft palate |
| R. G..... | 9/ 2/43 | Patent ductus arteriosus † | Cataract, right; deafness; mental retardation |
| E. P..... | 9/19/43 | Patent ductus arteriosus † | None |
| M. H..... | 10/ 4/43 | "Congenital heart" * | Deafness |
| P. M..... | 10/29/43 | Patent ductus arteriosus † | None |
| R. S..... | 11/ 3/43 | Patent ductus arteriosus † | Cataract, bilateral |
| S. A..... | 11/19/43 | Patent ductus arteriosus † | Cataract, right |
| C. W..... | 12/ 7/43 | ?Patent ductus arteriosus | None |
| M. J..... | 12/12/43 | ?Patent ductus arteriosus | Cataract, left;deafness; mental retardation; deformed toes |
| C. F..... | 12/25/43 | Patent ductus arteriosus | Cataract, left; microphthalmos; microcephaly |
| E. K..... | 12/26/43 | "Congenital heart" * | Cataract, bilateral |
| M. C..... | 1/13/44 | Patent ductus arteriosus † | None |
| L. R..... | 1/14/44 | Patent ductus arteriosus † | None |
| V. B..... | 2/25/44 | Fetal endomyocarditis ‡ | Cataract, bilateral; malformation of liver |
| S. P..... | 11/22/44 | Patent ductus arteriosus † | Cataract, left |
| M. G.§..... | 1/ 5/46 | ?Auricular septal defect | None |

* Unspecified cardiac anomaly.
† Patent ductus arteriosus divided.
‡ Patent ductus arteriosus was also reported as present at autopsy but, by definition, must be excluded from the study since the child lived only 4 months.
§ Maternal rubella occurred during second trimester of pregnancy. In all other cases maternal rubella occurred during the first trimester of pregnancy.

arteriosus (68.0%) among the 25 cases in which there was a positive history is significantly higher than the proportion (18.3%) among the 60 cases in which there was a negative history.

Details of each of the 25 cases [20] with a positive history of maternal rubella are given in Table 6. The birth dates of all these children occur only in the season of September through February (Chart 3). Of these 25 children, there are specific diagnoses of congenital heart anomalies in 18, of whom 17 (94.4%) have patent

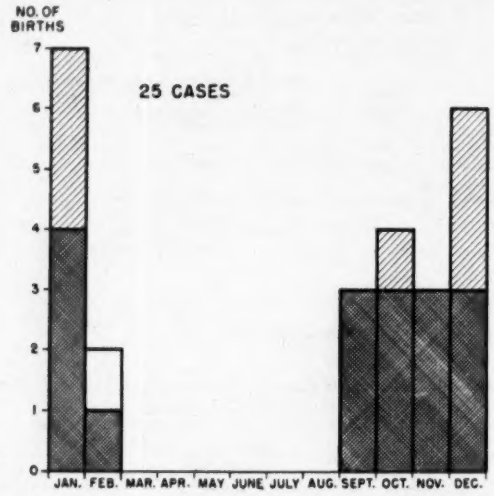


Chart 3.—Births by months of children with congenital heart disease and history of maternal rubella, Children's Hospital, Jan. 1, 1934, to Dec. 31, 1948. Hatched blocks indicate patent ductus arteriosus; slant lines indicate "congenital heart"; unshaded blocks indicate other congenital heart disease.

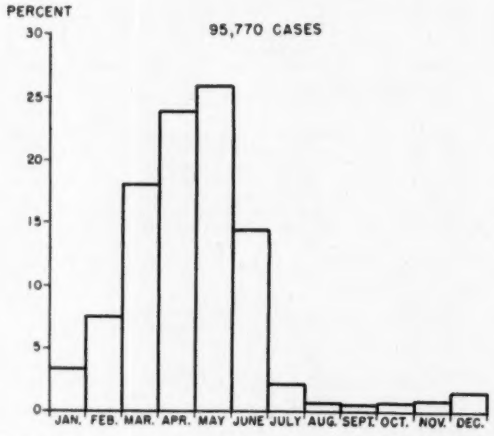


Chart 4.—Seasonal distribution of rubella in Massachusetts, 1934-1948; data obtained from Division of Communicable Diseases, Department of Public Health, Commonwealth of Massachusetts.

20. Four of these cases (P. S., E. K., L. R., and V. B.) have been reported previously (Dogramaci, I., and Green, H.: Factors in the Etiology of Congenital Heart Anomalies, J. Pediat. **30**:295-301 [March] 1947).

ductus arteriosus.[21] The most common noncardiac anomalies are congenital cataract (12 children) and deafness (6 children).

The unusual incidence of birth dates in the period, September through February, of these children with a positive history of maternal rubella is probably the result of the seasonal incidence of rubella in the late winter and spring months (Chart 4). In Massachusetts in the study years, 1934-1948, the peak months in incidence of rubella cases [22] were March (three years), April (three years), May (seven years), June (one year), and December [23] (one year).

Since congenital cataract is commonly associated with maternal rubella,[24] it was considered of interest to report upon the 19 children with both congenital cataract

TABLE 7.—*Children with Congenital Heart Disease and Congenital Cataract, Children's Hospital, Jan. 1, 1934-Dec. 31, 1948*

| Patient | Birth Date | Congenital Cardiac Anomalies | Other Congenital Anomalies | History of Maternal Rubella |
|---|---|---|---|---|
| P. S. | 1/11/34 | Septal defect | Cataract, right | Unknown |
| C. B. | 11/12/35 | "Congenital heart"* | Cataract, bilateral; cerebral malformation | Unknown |
| R. M. | 11/22/35 | ?Patent ductus arteriosus or septal defect | Cataract, bilateral; mental retardation | Unknown |
| G. D | 1/13/36 | "Congenital heart"* | Cataract, left; deafness | Yes |
| M. C. | 1/10/42 | Patent ductus arteriosus† | Cataract, bilateral | Yes |
| K. Z. | 10/27/42 | Patent ductus arteriosus† | Cataract, bilateral | Yes |
| M. H. | 11/12/42 | Patent ductus arteriosus †; hypoplasia of aorta | Cataract, left | Unknown |
| P. S. | 2/22/43 | Patent ductus arteriosus† | Cataract, right; harelip; cleft plate | Yes |
| F. K. | 3/21/43 | Patent ductus arteriosus | Cataract, bilateral | Unknown |
| R. G. | 9/ 2/43 | Patent ductus arteriosus† | Cataract, right; deafness; mental retardation | Yes |
| R. S. | 11/ 3/43 | Patent ductus arteriosus† | Cataract, bilateral | Yes |
| C. B. | 11/13/43 | ?Septal defect | Cataract, right | Unknown |
| S. A. | 11/19/43 | Patent ductus arteriosus† | Cataract, right | Yes |
| A. S. | 12/ 2/43 | Patent ductus arteriosus | Cataract, left | Unknown |
| M. J. | 12/12/43 | ?Patent ductus arteriosus | Cataract, left; deafness; mental retardation; deformed toes | Yes |
| C. F. | 12/25/43 | Patent ductus arteriosus | Cataract, left; microphthalmos; microcephaly | Yes |
| E. K. | 12/26/43 | "Congenital heart"* | Cataract, bilateral | Yes |
| V. B. | 2/25/44 | Fetal endomyocarditis‡ | Cataract, bilateral; malformation of liver | Yes |
| S. P. | 11/22/44 | Patent ductus arteriosus† | Cataract, left | Yes |

* Unspecified cardiac anomaly.
† Patent ductus arteriosus divided.
‡ Patent ductus arteriosus was also reported as present at autopsy but, by definition, must be excluded from the study since the child lived only 4 months.

and congenital heart disease. The details of each of these cases are given in Table 7. The birth dates of all of these children also have an unusual seasonal pattern, occur-

21. In the other case with a specific diagnosis, patent ductus arteriosus was also reported as present at autopsy but, by definition, must be excluded from the study, since the child lived only four months.

22. This evaluation is based upon the reported cases of German measles, Division of Communicable Diseases, Department of Public Health, Commonwealth of Massachusetts.

23. In 1934 the small peak of 148 cases in May was exceeded by the 328 cases in December which marked the beginning of an epidemic which reached a peak of 9,786 cases in the following May, 1935.

24. Gregg.[1] Swan.[4e]

ring in September through March only (Chart 5). Among these 19 children, 13 have specific diagnoses of congenital heart disease, 11 [25] (84.6%) of which are patent ductus arteriosus. A positive history of rubella is also present in the records in 12 cases, and a negative history of rubella in none of the cases. The unusual seasonal birth-date distribution directly related to the seasonal peak of rubella and the frequent occurrence of patent ductus arteriosus in these 19 cases are similar to those already noted among the 25 patients who had congenital heart disease and a positive history of maternal rubella.

## COMMENT

The birth-date distribution of children with patent ductus arteriosus (Chart 2) in all months of the year and the high seasonal incidence in the late autumn and early winter suggest that two types of patent ductus arteriosus might exist. The first type

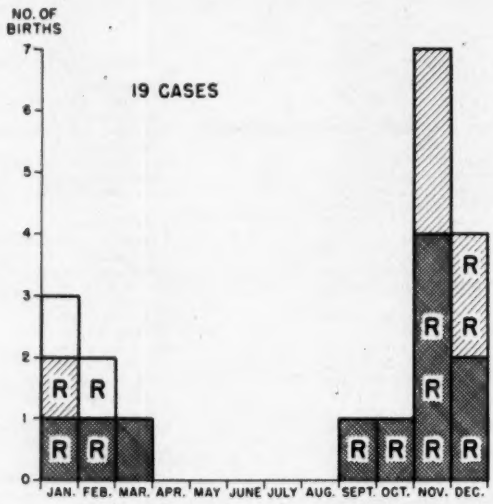


Chart 5.—Births by months of children with congenital heart disease and congenital cataract, Children's Hospital, Jan. 1, 1934, to Dec. 31, 1948. Hatched blocks indicate patent ductus arteriosus; slant lines indicate "congenital heart"; unshaded blocks indicate other congenital heart disease; *R* indicates rubella.

would consist of the majority of cases distributed more or less evenly throughout the year. The second type would be represented by the "excess" of cases in October through January produced by a seasonal factor, probably rubella.

The hypothesis that rubella is the environmental factor associated with the high seasonal incidence of patent ductus arteriosus, produced by the "excess" cases, is supported in this study by the following three "lines of evidence": (1) the unusual seasonal incidence in the late autumn and early winter of births of children with patent ductus arteriosus; (2) the peak incidence of rubella in Massachusetts in the late winter and early spring, which coincides with the first trimester of gestation

25. In one of the other two cases in which there was a specific diagnosis, patent ductus arteriosus was also reported as present at autopsy, but, by definition, must be excluded from the study since the child lived only four months.

of children born in late autumn and early winter, and (3) the births of children with a positive history of maternal rubella only in the months of September through February, the majority of which children have patent ductus arteriosus.

Patent ductus arteriosus is unique in that it is usually considered a postdelivery anomaly and not one present before birth. However, infection with the rubella virus may affect the anatomical design or the mechanism which closes or obliterates the ductus after birth. Swan,[26] in examining the patent ductus arteriosus of three cases in which autopsy was done, found that these differed structurally from the normal ductus (internal elastic lamina absent or ill-defined, larger lumen, thinner walls, some replacement of muscle by collagen fibers). There is need for further anatomical study of patent ductus arteriosus occurring after maternal rubella and comparison with those occurring without such a history. This was impossible in the present study, since autopsy or surgical specimens were not available.

## ADDITIONAL CASES [27]

After completion of this study, additional data were collected at Perkins Institution and Massachusetts School for the Blind (hereafter referred to as Perkins Institution). Records were studied of all children with congenital cataract who attended the school during the period, September, 1935, through January, 1951. This resulted in the discovery of eight patients with congenital heart disease previously unknown to us, for five of whom a specific diagnosis of patent ductus arteriosus was made, and six of whom have a history of maternal rubella during pregnancy. There were also two patients with congenital cataract and congenital heart disease who were previously included among those studied at the Children's Hospital. A positive history of maternal rubella in one of these two (F. K.) was recorded in the record at Perkins Institution but not in the Children's Hospital record.

When the data from Perkins Institution are combined with those from the Children's Hospital,[28] there are 32 children with congenital heart disease and a positive history of maternal rubella. As shown in Chart 6, the birth dates of these 32 children occur in the fall and winter months, September through March, with none in the period, April through August. Of these 32 cases, specific diagnoses of congenital heart disease were made in 23, in 22 (95.7%) of which the diagnosis was patent ductus arteriosus.

The addition of 8 new cases from Perkins Institution to the 19 identified at the Children's Hospital results in a total of 27 cases with congenital heart disease and congenital cataract. The birth dates of these 27 children also occur in the months September through March, with none in the period April through August (Chart 7). Of these 27, specific diagnoses of congenital heart disease were made for 18 and of patent ductus arteriosus for 16 (88.9%). A positive history of maternal rubella is present in the records of 19 [28] of the 27 cases. As illustrated by Charts 6

26. Swan, C.: A Study of 3 Infants Dying from Congenital Defects Following Maternal Rubella in the Early Stages of Pregnancy, J. Path. & Bact. **56**:289-295 (July) 1944.

27. Dr. Gabriel Farrell, former Director, Dr. Trygve Gundersen, Ophthalmologist, and the staff, Perkins Institution and Massachusetts School for the Blind, gave us their cooperation in making the records of the institution available to us.

28. Now including F. K. for whom a positive history of maternal rubella was recorded at Perkins Institution.

Chart 6.—Births by months of children with congenital heart disease and history of maternal rubella, Children's Hospital and Perkins Institution, Jan. 1, 1934, to Dec. 31, 1948. Hatched blocks indicate patent ductus arteriosus; slant lines indicate "congenital heart"; unshaded blocks indicate other congenital heart disease.

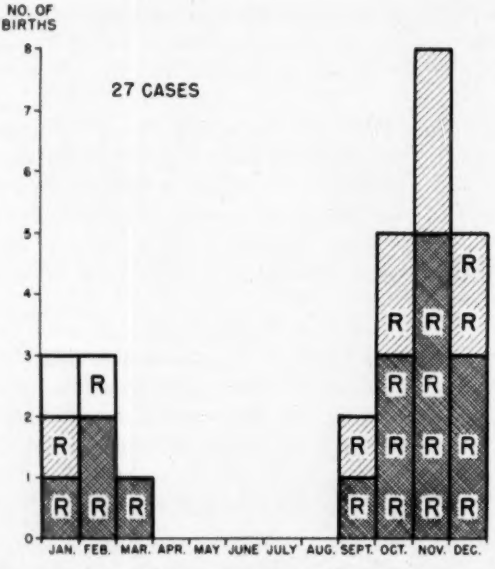


Chart 7.—Births by months of children with congenital heart disease and congenital cataract, Children's Hospital and Perkins Institution, Jan. 1, 1934, to Dec. 31, 1948. Hatched blocks indicate patent ductus arteriosus; slant lines indicate "congenital heart"; unshaded blocks indicate other congenital heart disease; *R* indicates rubella.

and 7, the addition of the eight cases from Perkins Institution to those studied at the Children's Hospital makes the unusual seasonal birth-date distribution more striking and strengthens the implication of a relationship between maternal rubella and patent ductus arteriosus.

SUMMARY

The births, tabulated by month and by specific diagnosis, of 1,042 children with congenital heart disease diagnosed at the Children's Hospital were compared with the birth-date distribution of all live births in Massachusetts for the same period, 1934-1948.

The births of the 1,042 children with congenital heart disease have an increased seasonal incidence in the period October through January, which differs significantly from that of all live births in Massachusetts (1934-1948).

Births of all children with congenital cardiac anomalies other than patent ductus arteriosus and, more specifically, of those with septal defect, tetralogy of Fallot, or coarctation of aorta, are distributed more or less evenly throughout the year.

Births of children with patent ductus arteriosus have a distinct seasonal distribution in the months October through January. The first trimester of gestation of these children occurs in late winter and early spring and coincides with the season of high incidence of rubella in Massachusetts.

Births of the 25 children with congenital heart disease and a positive history of maternal rubella occur in the months September through February only. Among these 25 cases, in 18 specific diagnoses of congenital heart disease have been made, 17 of which are patent ductus arteriosus.

The additional data collected at Perkins Institution and Massachusetts School for the Blind, supplementing those from the Children's Hospital, makes the results of this study more meaningful.

The results of this study suggest that the seasonal "excess" of cases of patent ductus arteriosus is due to a seasonal environmental factor, probably rubella. Conclusive proof of this thesis is dependent on a "forward inquiry" correlating the occurrence of specific congenital cardiac anomalies with maternal rubella.

Dr. Jane Worcester, Associate Professor of Biostatistics, Harvard School of Public Health, and Dr. Williams E. Reynolds, Instructor in Preventive Medicine, Harvard Medical School, gave advice and guidance in the analysis of the data presented.

# FURTHER ELECTROENCEPHALOGRAPHIC STUDIES IN SICKLE CELL ANEMIA

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AND
BILLIE CAMP DAVIS, B.S.
MEMPHIS

IN A PREVIOUS communication,[1] the electroencephalographic findings in sickle cell anemia were reported. Included in this study were eight patients who presented an exacerbation of the symptomatology of sickle cell disease and who, therefore, were considered to be in a state of sickle cell crisis. Since the electroencephalograms were abnormal for all eight of these patients, we felt that further evaluation of electroencephalographic patterns of patients with sickle cell crisis was indicated.

It is the purpose of this paper to present a heretofore unreported electroencephalographic finding and to analyze the electroencephalograms of 12 additional patients who had been hospitalized with signs and symptoms of sickle cell crisis. Evidence has been presented previously to correlate the nature of brain potentials with clinical manifestations in those patients with central nervous system symptoms of sickle cell anemia.

## METHODS

The diagnosis of sickle cell anemia was established definitely in each case before it was included in the series. If there was any doubt that the patient was in crisis, as determined by the presence of fever, jaundice, or pain in a patient known to have sickle cell disease, he was excluded from the study.

Electroencephalograms were obtained under standard conditions to assure valid tracings. The machine used was an Offner Type C 144 four-channel crystograph electroencephalograph. No sedative agents were given. Eight scalp electrodes were used in the following positions: two frontal, two parietal, two occipital, and two temporal. Electrodes were attached to each ear for use as reference points. Standard scalp-to-ear and scalp-to-scalp leads were employed. Whenever an abnormality was noted in a particular area, more sensitive triangulation techniques were used to localize more sharply the site of the abnormality.

Electroencephalograms were interpreted according to the Davis system.[2] The classification of alpha index was based upon the scales set up by Lindsley [3] and Bernhard and Skoglund [4] for

Supported by a grant from the United States Public Health Service.

From the Pediatric Division, University of Tennessee College of Medicine, and the John Gaston Hospital.

1. Hill, F. S.; Hughes, J. G., and Davis, B. C.: Electroencephalographic Findings in Sickle Cell Anemia, Pediatrics **6**:277, 1950.

2. Davis, P. A.: Technique and Evaluation of the Electroencephalogram, J. Neurophysiol. **4**:92, 1941.

3. Lindsley, D. B.: Electrical Potentials in Brain of Children and Adults, J. Gen. Psychol. **19**:285, 1938; Longitudinal Study of Occipital Alpha Rhythm in Normal Children: Frequency and Amplitude Standards, J. Genet. Psychol. **55**:197, 1939.

4. Bernhard, C. G., and Skoglund, C. R.: On Alpha Frequency of Human Brain Potentials as Function of Age, Skandinav. Arch. Physiol. **82**:178, 1939.

children of various ages. This was done in order to differentiate waves in the slow frequency range commonly considered to be abnormal from those which are, in reality, normal for children of various age groups. The studies made by Gibbs and Gibbs were used as the criteria for determining normality in sleep.[5]

In addition to the usual admission history and physical examination, special consideration was given to the nervous system. Electroencephalograms and hemoglobin levels were obtained on all patients before any necessary blood transfusions were given.

## RESULTS

A summary of the significant findings for all the patients is presented in the accompanying table. The electroencephalograms were abnormal in all patients studied. However, two patients presented asymmetry of the hemispheres, a finding not heretofore noted in the electroencephalographic patterns of patients with sickle cell disease. Both exhibited unusual and interesting neurological signs.

The first patient was an 8-year-old Negro girl who was known to have sickle cell disease. She was admitted to the hospital with a right-sided hemiplegia of two

*Signs and Symptoms of Patients with Sickle Cell Anemia*

| Patient | Age, Yr. | Sex | Hemoglobin, Gm./100 Cc. | Fever | Icterus | Anorexia | Abdominal Pain | Hepatomegaly | Splenomegaly | Edema | Vomiting | Lethargy | Hemiplegia | Irritability | Fatigue | Convulsion | Pain in Legs | Abnormal EEG |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C. D. | 9 | M | 8 | .. | + | .. | .. | .. | .. | + | .. | .. | .. | .. | .. | .. | .. | + |
| L. H. N. | 4 | M | 6 | + | + | + | + | + | .. | .. | .. | .. | .. | .. | .. | .. | .. | + |
| T. T. | 5 | M | 7 | + | + | + | + | .. | .. | .. | .. | .. | .. | .. | .. | .. | + | + |
| L. R. | 2 | M | 9.5 | + | + | .. | + | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | + |
| W. S. | 4 | M | 3 | + | + | + | + | + | + | .. | + | .. | .. | .. | .. | .. | .. | + |
| T. Th. | 1½ | M | 5.5 | + | + | .. | .. | .. | + | + | .. | .. | .. | .. | .. | .. | .. | + |
| B. W. | 8 | F | 5 | + | .. | + | + | .. | .. | .. | + | .. | .. | .. | .. | .. | .. | + |
| A. F. | 7 | M | 7.5 | + | .. | .. | .. | + | .. | .. | .. | + | .. | .. | + | .. | .. | + |
| A. A. | 5 mo. | F | Less than 7 | + | .. | + | .. | .. | .. | + | .. | .. | .. | .. | .. | .. | .. | + |
| C. C. | 4 | F | 7 | + | .. | .. | .. | + | + | .. | .. | .. | .. | + | .. | .. | .. | + |
| A. S. | 8 | F | 10.5 | + | .. | .. | .. | .. | .. | .. | .. | .. | + | .. | .. | .. | .. | + |
| H. H. | 14 mo. | F | Less than 7 | + | .. | .. | .. | .. | .. | .. | + | + | + | .. | .. | + | .. | + |

days' duration but with no sensory loss. Figure 1 illustrates the marked asymmetry seen in the electroencephalogram, which was recorded within 12 hours after admission. Another electroencephalogram taken 32 days later showed a diminution of asymmetry (Fig. 2). At this time there had also been clinical improvement. When discharged from the hospital 10 days after the last electroencephalogram, the patient was able to walk, although flexion of the right leg was still impaired.

The second patient was a 19-month-old Negro girl who was admitted to the hospital with the chief complaint of weakness of the right leg. The red blood cell count was 1,730,000, the hemoglobin concentration less than 7.5 gm. per 100 cc., and numerous sickle cells were seen on the blood smear. Results of examination of the spinal fluid were negative. This patient had a febrile clinical course characterized by marked lethargy and right-sided convulsions which occurred for the first time on the eighth hospital day. Although amobarbital (amytal®) sodium was administered,

5. Gibbs, E. L., and Gibbs, F. A.: Electroencephalographic Changes with Age During Sleep; abstracted in Electroencephalog. & Clin. Neurophysiol. **2**:355, 1950.

the convulsions occurred intermittently for the next 48 hours. The electroencephalographic findings were essentially the same as those of the first patient. The patient was discharged on the 25th hospital day and was found to have no neurological sequelae when observed in the outpatient clinic six months later.

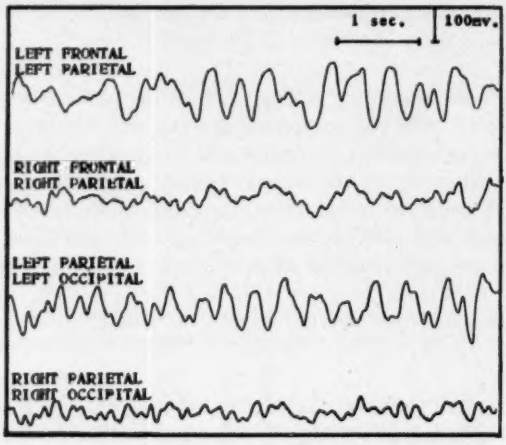


Fig. 1.—Scalp-to-scalp tracing, showing marked asymmetry.

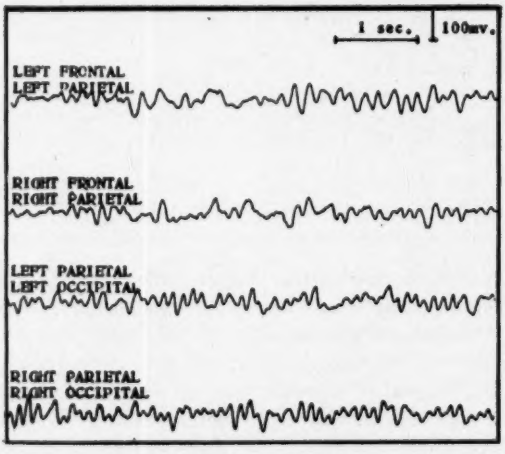


Fig. 2.—Scalp-to-scalp tracing, on same child as in Figure 1 done 32 days later, showing diminution of asymmetry.

The most characteristic electroencephalographic findings were generalized instability, sharp waves of high microvoltage, and a predominance of slow activity. Phase reversals were noted in all tracings, especially over the occipital areas. Suppression of cortical electrical activity was observed in only five patients; it was intermittent and appeared most frequently over the frontal and temporal regions. The scalp-to-ear and scalp-to-scalp tracings showed no difference in degree of cere-

bral dysrhythmia. These results correlate closely with those observed in patients studied previously.

## COMMENT

Patients with crises of sickle cell disease have exacerbations of symptoms and, thus, more pronounced pathologic lesions than those in asymptomatic phases. Since sickle cell anemia is an occlusive vascular disease, generalized tissue anoxia will occur any time the pathologic forces of this condition are at play. It follows that more widespread and severe tissue changes in the brain would result in greater degrees of cerebral anoxia. It was not unexpected, therefore, that all the patients in this series presented abnormal electroencephalograms.

An analysis of the table reveals several interesting and significant observations regarding the relationship of electroencephalographic patterns to clinical features presented by patients with the crisis of sickle cell disease. Of the symptoms manifested by the group of patients in this study, abdominal pain, vomiting, hemiplegia, pain in the legs, lethargy, irritability, and convulsions were considered to be possibly related to central nervous system involvement. All but three patients had one or more of these symptoms. However, as noted previously, all of the electroencephalograms obtained on these patients were abnormal. This indicates that subclinical involvement of the central nervous system may occur and that electroencephalography affords a more sensitive technique for determining in such patients the presence of pathologic processes which result in cerebral dysrhythmia.

Several authors have described the changes observed in the nervous system, all of which are thought to cause anoxia with consequent cortical dysfunction. The vascular changes which result in anoxia may be ascribed to functional obstruction of blood vessels [6] or to thrombotic occlusion of arteries.[7]

No correlation was apparent between hemoglobin levels and electroencephalographic abnormalities or clinical manifestations. One of the most severely ill patients had a hemoglobin concentration of 10.5 gm. per 100 cc. This is further evidence that marked hemolysis of red blood cells is not always the principal underlying process in the crises of sickle cell disease.

## SUMMARY AND CONCLUSIONS

Electroencephalographic findings of 12 patients who had been hospitalized with signs and symptoms of sickle cell crisis are presented.

The electroencephalograms were abnormal for all 12 of these patients, although 3 of the patients did not present symptoms possibly referable to the central nervous system.

A finding not previously observed in the electroencephalographic patterns in earlier studies on sickle cell disease was the appearance of asymmetry of the hemispheres.

Study of patients with sickle cell crisis by means of electroencephalography is of valuable assistance in determining the effect that pathologic changes may have on cortical function.

20 S. Dunlap.

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6. Kimmelstiel, P.: Vascular Occlusion and Ischemic Infarction in Sickle Cell Disease, Am. J. M. Sc. **216**:11, 1948.

7. Hughes, J. G.; Diggs, L. W., and Gillespie, C. E.: Involvement of the Nervous System in Sickle Cell Anemia, J. Pediat. **17**:166, 1940.

# Case Reports

## CAT-SCRATCH FEVER ENCEPHALITIS

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WASHINGTON, D. C.

THIS IS a report of the first case of encephalitis associated with cat-scratch fever ever described. Over 100 cases [1] of this newly described syndrome of cat-scratch fever have been reported in the world's literature. In all instances the authors uniformly have emphasized the benign and self-limiting nature of the illness, and none has suggested the possibility of neurotropic activity of the unidentified virus. None has described the prolonged coma, prostration, convulsions, and neurological involvement observed in the case summarized here.

Although Dr. Lee Foshay of Cincinnati is credited with defining this clinical entity and developing the skin test for it, most of the articles on cat-scratch fever emanate from French medical centers,[2] only five articles appearing in American medical journals.[3] The origin of cat-scratch fever is not definitely proved, and the isolation of the virus and reproduction of the disease in animals have not been achieved to the satisfaction of most of the workers in the field. With a few exceptions,[4] most authorities implicate a cat scratch or bite as the causative event in the preponderance of cases. The cat scratch or bite is followed in a few days by a circumscribed and usually indolent ulcer at the injured site, with secondary enlargement of the local

Associate Professor of Neurology, Georgetown University Medical School.

Presented before the Annual Scientific Meeting of the Jacobi Medical Society.

1. Daniels, W. B., and MacMurray, F. G.: Cat-Scratch Disease, Arch. Int. Med. **88**:736-751, 1951.

2. (*a*) Debré, R.; Lamy M.; Jammet, M. L.; Costil, L., and Mozziconacci, P.: La maladie des griffes de chat, Bull. et mém. Soc. Méd. hôp. Paris **66**:76-79, 1950; (*b*) La maladie des griffes de chat, Semaine hôp. Paris **26**:1895, 1950. (*c*) Drovet, P. L.; Faivre, G., and Craus, B.: Premiers cas lorrains de la "maladie des griffures de chat," Rev. méd. Nancy **75**:487-491, 1950. (*d*) Lemaire, A., and Debray, J.: Sur une épidémic familiale d'adénite subaigue bénigne de nature inconnue, Bull. et mém. Soc. méd. hôp. Paris **66**:375-378, 1950. (*e*) Mahoudeau, D.; Lemperiere, E., and Leroux, G.: Un nouveau cas de polyadénopathie subaigue paraissant consécutive a des griffures de chat, ibid. **66**:410-412, 1950. (*f*) Mollaret, P.; Reilly, J.; Bastin, R., and Tournier, P.: Sur une adénopathie régionale subaiguë et spontanément curable, avec intradermo réaction et lésions ganglionaires particulières, ibid. **66**:424-449, 1950; (*g*) Documentation nouvelle sur l'adénopathie régionale subaiguë et spontanément curable décrite en 1950: la lymphoréticulose bénigne d'inoculation, Presse méd. **58**:1353-1355, 1950; (*h*) Une maladie ganglionnaire nouvelle: adénopathie régionale subaiguë spontanément curable avec intradermo réaction et lésions histologiques particulières, ibid. **58**:282-283, 1950; (*i*) La découverte du virus de la lymphoréticulose bénigne d'inoculation, ibid. **59**:681 and 701, 1951. (*j*) Paraf, J., and Fournier, E.: Nouveau cas d'adénopathie par griffes du chat, Bull. et mém. Soc. méd. hôp. Paris **66**:539, 1950. (*k*) Thelin, F., and Martin-du-Pan, R.: New Observation of Diseases Due to Cat Scratches, Praxis **40**:74, 1951.

3. (*a*) Daniels and MacMurray.[1] (*b*) Bennett, I. L., and Melton, J. T.: Cat-Scratch Disease, Georgia M. A. J. **40**:466, 1951. (*c*) Blattner, R. J.: Cat-Scratch Fever, editorial, J. Pediat. **39**:123-124, 1951. (*d*) Greer, W. E. R., and Keefer, C. F.: Cat-Scratch Fever: A Disease Entity, New England J. Med. **244**:545-548, 1951. (*e*) Lange, H. L.: Cat-Scratch Fever: A Report of 3 Cases, J. Pediat. **39**:431-434, 1951.

4. Lemaire and Debray.[2d] Thelin and Martin-du-Pan.[2k]

lymph nodes which eventually become flocculent and may continue to suppurate for weeks or months. Both the original lesion and the involved lymph nodes are bacteriologically sterile upon direct smear and culture. Animal inoculations fail to propogate the disease or to yield the offending virus, although one recent report [21] purports to show inclusion bodies which are allegedly typical histological phenomena of this disorder. Clinical diagnosis of cat-scratch fever is confirmed by the intradermal injection of 0.1 cc. of dilute sterilized pus from a lymph node of a patient with the disease, similar to the Frei-test technique. A positive complement-fixation reaction of the blood serum further supports the diagnosis.[5]

A mild systemic reaction occasionally occurs in typical cat-scratch disease. Infrequently a transient skin eruption develops,[6] as also occurred in the case reported below.

## REPORT OF A CASE

L. H., a 13-year-old white boy, had been under the usual pediatric surveillance at the Group Health Clinic; development was normal, and, aside from a multiplicity of childhood diseases, he had been well until March 17, 1949, when he suffered headache, and a temperature of 100.4 F. was noted. At the same time a small, crusted papule was present on the right forearm, and the epitrochlear and particularly the axillary lymph nodes were enlarged and tender on the right side. The rest of the findings on examination were normal. The blood cell count on March 19 showed 22,250 white cells, with 38% polymorphonuclear leucocytes, 6% eosinophiles, and 56% lymphocytes; the hemoglobin value was 14 gm. The same day 300,000 units of penicillin was administered. Intermittent but increasing fever ensued, unresponsive to further penicillin and sulfadiazine therapy. One week after the onset the patient had a generalized convulsion, lapsed into deep coma and was admitted March 25 to the Children's Hospital, with a temperature of 105.4 F., pulse rate of 120, and respiration rate of 30 per minute (Fig. 1).

The neurological examination on that day revealed a restless, comatose, well-developed boy, who was incontinent of urine and feces. The head was rotated to the left but could be passively turned to the right. There was no bruit and no scars. The neck was markedly rigid, and passive attempts to move it caused the patient to groan. Kernig's sign was present. The right arm was held in flexion at the elbow and was weak. The cranial nerves revealed normal optic disks aside from moderate congestion. There were no exudates, hemorrhages, or papilledema. Opticokinetic reflexes were normal, but the eyes showed left conjugate lateral deviation; the pupils reacted normally. There was a right central facial weakness of moderate degree. The palate, uvula, and tongue appeared normal. There was a bilateral Babinski reflex, stronger on the left. The skin showed pale erythematous flat coalescent lesions on the trunk, and a small raised papule was noted on the right forearm, suggesting a bite to the examiner. A diagnosis of encephalitis, probably virus, was made.

The eruption described above faded in the next two days, but the axillary lymph node on the right increased to the size of a large olive. Generalized convulsions, at times proximating status epilepticus, continued in spite of large intramuscular doses of phenobarbital sodium, and several paroxysms of opisthotonos, typical of mesencephalic seizures, were observed. The temperature rose to 106.4 F., but after the administration of aureomycin fever and clinical symptoms showed a rapid defervescence. Forty-eight hours after aureomycin was administered, the temperature was normal and the patient was lucid. He was discharged from the hospital on March 31, 1949.

From laboratory studies the following results were obtained. During the acute illness two lumbar punctures were performed, one upon admission and one on the succeeding day; in both instances the results were negative in every respect. Cerebrospinal fluid was examined for virus at the National Institutes of Health, and the results were negative. There was no laboratory evidence of lymphocytic choriomeningitis. There were no neutralizing antibodies against St. Louis (Type C epidemic) encephalitis or against the virus of eastern or western equine encephalomyelitis. Results of agglutinization tests were negative for Brucella abortus, Brucella militensus, Pasteurella tularensis, Proteus X19, and Salmonella (Eberthella) partyphi A and B. The hetero-

5. Armstrong, Charles: Personal communication to the author.

6. Blattner.[3c] Greer and Keefer.[3d]

phile antibody reaction was negative. Repeated tuberculin skin tests elicited negative reactions. Roentgenograms of the chest and skull were normal on April 22, 1949.

The right axillary lymph node enlarged, reaching the size of a small egg, and suppurated. On May 9 about 12 cc. of greenish pus was aspirated from the axillary abscess and examined. There was an abundance of pus cells, a few red blood cells, some epithelial cells, and a large amount of fibrin; no organisms were found. The reaction to acid-fast stain was negative, and a concentration test revealed no tubercle bacilli. No growth was obtained upon repeated culture. The pus was inoculated intraperitoneally and subcutaneously in guinea pigs, and the animals were

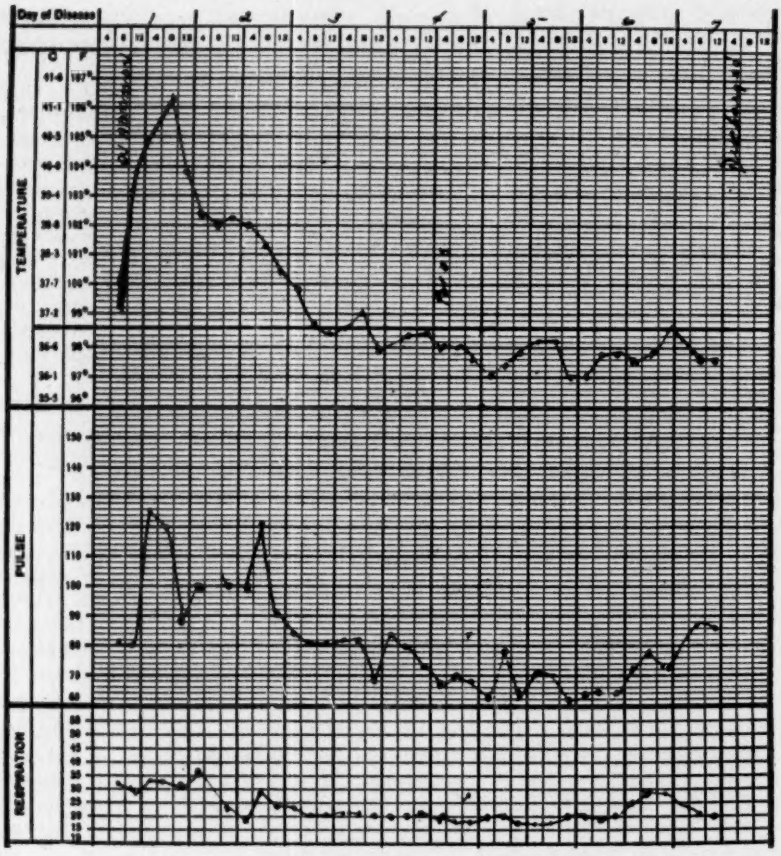


Fig. 1.—Chart of patient's temperature, pulse, and respirations.

killed and autopsies done about six weeks later. There was no evidence of tuberculosis or tularemia in the animals. The axillary node continued to drain for the next three months, slowly healing.

Results of follow-up neurological examinations remained negative, although the mother reported that the patient tended to drag his left leg slightly for several weeks after discharge from the hospital. The patient was unusually restless, irritable, and readily fatigued and nightmares developed for several weeks after the acute illness subsided. An electroencephalogram (Fig. 2), done one month after admission to the hospital, showed frequent random slow waves, appearing in isolation and in brief synchronous bursts, usually of four-per-second frequency. The

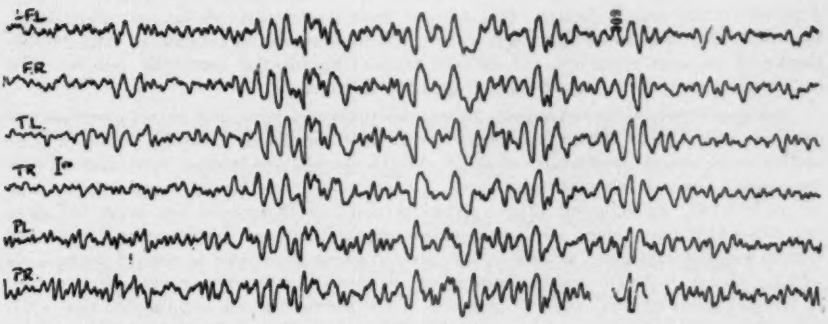


Fig. 2.—Electroencephalogram about five weeks after onset of encephalitis; paired frontal, temporal, and parietal leads; waking record.

Fig. 3.—Skin-test reaction after 48 hours; performed more than two and one-half years after acute illness.

tracing was considered to be abnormal and consistent with a diagnosis of convulsive disorder. A repeat tracing done in January, 1951, showed much less dysrhythmia but was still slightly abnormal. There was no focus in either instance. There have been no convulsions since the subsidence of the acute symptoms, and the mild behavior disorder has completely resolved. The patient is a robust, energetic, and well-adjusted boy at present.

As a consequence of the recent publication of descriptions of cat-scratch fever,[1] a retrospective diagnosis was made over two and one-half years after the illness occurred. One-tenth cubic centimeter of antigen, kindly supplied by Dr. Worth Daniels, was injected subcutaneously into the patient. The test was read in 48 hours, at which time a reaction measuring 3 in. by 3 in. (8 cm. by 8 cm.) was observed (Fig. 3), which persisted for 10 days and then faded; but about two weeks after the injection a raised, indurated, painful, turgescent papule gradually appeared, with a widening erythematous aureola, the latter reaching dimensions of about 1 in. by 2 in. (2.5 cm. by 5.0 cm.). This papule persisted for six weeks, and for further serologic tests 1 cc. of serosanguinous material was aspirated from it one month after the original skin test. This late and persistent papular lesion following the skin test has been described by French workers.[7] In addition, the skin test invoked a mild febrile and systemic reaction.

Blood serum was sent to the National Institutes of Health on Dec. 31, 1951, for a complement-fixation test. This was positive in 1:32 dilution which, according to Dr. Charles Armstrong, is the highest titer that he has observed. Upon further questioning, the patient recalled being scratched many times by his pet cat before and after his illness, but he cannot recall the details.

## COMMENT

I believe the diagnosis of cat-scratch fever, although retrospective, is clearly established. The marked skin reaction and the strongly positive complement fixation, even though more than two and one-half years had elapsed since onset, suggest the possibility of an unusually heavy inoculation. This might also account for the development of encephalitis which, as stated, has not been observed previously in this disease. The clinical manifestations are also quite typical, including history of a cat scratch, development of a local indolent ulcer, and enlargement and suppuration of the local axillary lymph node which yielded no organism upon smear, culture, animal inoculation, etc. The response to aureomycin and the failure of penicillin to be effective have also been described as characteristic.[2a] The transient skin eruption is a common occurrence also.

The concomitant encephalitis has also been established by the severe and multiple convulsions; neurological findings, including nuchal rigidity; the abnormal electroencephalogram, and sequela of behavior disorder. The causal relationship is inferential, but it appears justified by the complete negativity of results of all studies attempting to implicate the commoner causes of encephalitis. In addition, it is important to note that this child had already had the usual exanthematous diseases which are known to produce the complication of encephalitis.[8] The last such exanthematous disease was five years before the cat-scratch fever was contracted, and these diseases included scarlet fever, mumps, rubeola, rubella, chickenpox, roseola, and pertussis. Vaccination against smallpox was done at 2 years of age.

## SUMMARY

The first case of cat-scratch fever associated with encephalitis is described. Penicillin was typically ineffectual, but the use of aureomycin was followed by prompt defervescence of symptoms and fever. All previous reports have emphasized the benign character of cat-scratch fever, but the possibility of the complication of encephalitis should be considered.

3315 Sixteenth St. N.W.

7. Footnote 2*a* and *b*.

8. Neal, J. B., and others: Encephalitis, New York, Grune & Stratton, Inc., 1942.

# CONGENITAL TOXOPLASMOSIS OCCURRING IN IDENTICAL TWINS

LIEUTENANT (jg) WILLIAM F. MURPHY (MC), U.S.N.R.
AND
CAPTAIN JOHN L. FLANNERY (MC), U.S.N.

THE FOLLOWING cases of congenital toxoplasmosis are presented to illustrate a deviation from the general pattern of signs and symptoms that ordinarily occur in this disease, as well as the fact that the disease was transmitted by the mother to her identical twins.

Toxoplasmosis has been described previously in identical twins by Zuelzer [1] in 1944 and by Abbott and Camp [2] in 1947. The disease has been reported in binovular twins by Bamatter [3] in 1947 and by Farquhar [4] in 1950.

## REPORT OF CASES

CASE 1.—Charles W. M., the first of identical twins, weighing 5 lb., 14 oz. (2,700 gm.), was born by cephalic presentation at term to a healthy primigravida 22-year-old woman on Aug. 11, 1947. The patient and the mother were discharged from the hospital in good condition on the sixth postpartum day. The infant thrived on evaporated-milk formula and routine infant care. When he was 2 months old the mother noticed a constant bilateral esotropia. This, however, was dismissed by helpful neighbors, who suggested that it was a normal occurrence in young babies. When the infant was 4 months old a horizontal nystagmus developed. It was not, however, until the child was 20 months old that medical advice was sought for the eye complaints.

The child was admitted to the United States Naval Hospital, Portsmouth, Va., on Aug. 10, 1949, with the diagnosis of esotropia. On his second birthday, a Reese resection was done on his left eye, with the patient under ether anesthesia. The child was discharged five days later after a satisfactory hospital course. There was a decided improvement in the esotropia and nystagmus following the surgery. The child developed normally, but now, in retrospect, the parents feel that he probably did have difficulty in vision, in that he would run into large objects from time to time.

On June 22, 1950, he was found in a semilucid state. Whenever the child attempted to stand, he would fall to his right side. He was immediately taken to the emergency room at the United States Naval Hospital, where a lumbar puncture was done. The cerebrospinal fluid was reported to be normal, and the child was returned home. He slept for an hour or so and then resumed his normal play. He remained well until Dec. 10, 1950, when a similar episode

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This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the authors and are not to be construed as reflecting the policies of the Navy Department.

1. Zuelzer, W. W.: Infantile Toxoplasmosis, with Report of 3 New Cases, Including 2 in Which Patients Were Identical Twins, Arch. Path. **38**:1-19 (July) 1944.

2. Abbott, K. H., and Camp, J. D.: Extensive Symmetrical Cerebral Calcification and Choroidoretinitis in Identical Twins (Toxoplasmosis): Clinical Report of Cases, Bull. Los Angeles Neurol. Soc. **12**:38-47 (March) 1947.

3. Bamatter, F.: La chorioretinite toxoplasmique, Ophthalmologica **114**:340-358 (Oct.-Nov.) 1947.

4. Farquhar, H. G.: Congenital Toxoplasmosis: Report of 2 Cases in Twins, Lancet **2**:562-564 (Nov. 18) 1950.

occurred. As before, the child slept for an hour, then seemed completely recovered. The patient was admitted to the hospital on Dec. 13, 1950, for diagnostic study.

*Family History.*—The father was 28 years old, native-born of Greek parents. He was a robust chief patternmaker. He could recall no illnesses. The mother too, was a very healthy woman, 25 years old, of Anglo-Saxon parentage. She had not been ill during her pregnancy or prior to it. She had worked in a meat-packing plant, making frankfurters in 1944 for a period of three weeks. She was employed as a waitress from 1944 until 1946.

*Physical Examination.*—Charles W. M. was a well-developed, slightly obese child (Fig.), 3 years old, active, and mentally alert. A constant horizontal nystagmus was present. The pupils reacted normally to light. Examination of the fundi revealed an extensive choroido-

Charles W. M. (Case 1) (left) and Chester W. M. (Case 2) (right) at 3 years, 7 months of age. (Official Photograph of the United States Navy)

retinitis with atrophy of the optic disk. The lungs, heart, and abdomen appeared normal. Results of neurological examination were considered normal by the consultant neurologist.

*Laboratory Data.*—The urine was normal. The red blood cell count was 4,200,000, with a hemoglobin value of 12.5 gm. (86%), and the white blood cell count was 8,700, with the following differential distribution: 44% neutrophils, 40% lymphocytes, 13% monocytes and 3% eosinophils. The serum-calcium value was 13 mg. per 100 cc., and the fasting blood-sugar reading was 64 mg. per 100 cc. The roentgenogram of the skull showed no evidence of intracerebral calcification. Electroencephalographic examination suggested a lesion in the right frontal area. Funduscopic examination by the ophthalmology department revealed an extensive choroidoretinitis. It was suggested that the presence of toxoplasmosis should be ruled out. The patient was discharged from the hospital on Dec. 19, 1950, to be followed in the outpatient department.

A specimen of blood was collected from the patient, his twin, and his mother, and sent to the United States Naval Medical School, Bethesda, Md., for studies of complement fixation and a dye test against toxoplasmosis. The complement fixation was reported positive, and the results of the dye test were positive in dilutions of 1:1,024 (Table). Several follow-up roentgenograms of the skull have revealed no abnormalities. In no incidence was there any evidence of intracerebral calcification (Table).

On March 21, 1951, the patient, his twin, and a younger brother were admitted to the hospital for one night for lumbar punctures. The cerebrospinal fluid was normal in each case (Table).

The patient remained well, except for visual difficulties, until Sept. 19, 1951, at which time he had a convulsive seizure. Anticonvulsive therapy was begun, and to date no further seizures have occurred.

CASE 2.—Chester W. M. was born two minutes later than his identical twin, by breech presentation. He weighed 4 lbs., 11 oz. (2,150 gm.). At approximately 2 months of age, estropia developed in this child too, but nystagmus was less noticeable. He was admitted to the hospital

*Laboratory Data on Identical Twins, Mother, and Siblings*

| | Charles W. M. | Chester W. M. | Mother | J. E. M. | D. R. M. |
|---|---|---|---|---|---|
| Skull roentgenogram | 12/14/50 Normal | ..... | ..... | ..... | ..... |
| | 1/17/51 Normal | 1/22/51 Normal | | | |
| | 3/16/51 Normal | 3/16/51 Normal | | 3/16/51 Normal | |
| | 9/6/51 Normal | 9/6/51 Normal | | | |
| | 12/10/51 Normal | 12/10/51 Normal | | | |
| Complement fixation | 1/17/51 Positive | 1/17/51 Positive | 1/17/51 Positive | 4/11/51 Negative | 7/3/51 Negative |
| Dye test (titer) | 1/17/51 Positive (1:1,024) | 1/17/51 Positive (1:256) | 1/17/51 Positive (1:256) | 4/11/51 Negative | 7/3/51 Negative |
| Cerebrospinal fluid | 3/21/51 Normal | 3/21/51 Normal | ..... | 3/21/51 Normal | ..... |
| Electroencephalogram | 12/14/50 Suggested right-side lesion | ..... | ..... | ..... | ..... |
| | 10/1/51 Suggested left-side lesion | | | | |

when 2 years old, and a Reese resection was performed on his left eye for esotropia. A satisfactory result was recorded. He was admitted again on the same dates as his twin for diagnostic study. The physical examination revealed no abnormalities except in the eye, in which the findings consisted of esotropia, horizontal nystagmus, and choroidoretinitis. The choroidoretinitis was, however, less marked than was found in his twin. The complement fixation was positive, and the results of the dye test were positive in dilutions of 1:256.

The patient has been entirely well all his life, until Feb. 9, 1951, when he had what was considered to be a convulsive seizure, judged from the history given by the parents. He was weak on the right side immediately afterwards, but one hour later he had made a complete recovery. Repeated roentgenograms of the skull have been reported normal (Table). The patient has had no subsequent seizures. He presently receives ¼ grain (15 mg.) of phenobarbital three times a day, on the recommendation of the neurology department. At present he is leading a very active, healthy life, limited slightly by his visual impairment.

Two younger boy siblings have been born to the parents of the twins. J. E. M. was born spontaneously, weighing 6 lb., 15 oz. (3,100 gm.) on March 25, 1949.

D. R. M. was born normally June 29, 1951. He weighed 7 lb., 9½ oz. (3,400 gm.). As would be expected, neither of these children have shown any clinical or serological evidence of toxoplasmosis.

## SUMMARY

Two cases of toxoplasmosis occurring in identical twins have been presented. Clinical evidence of the disease was manifested by convulsive disorders and visual disturbances, namely, esotropia and nystagmus. Funduscopic examination revealed extensive choriodoretinitis in both cases. Serological evidence of the disease was proved by positive complement fixation and high-dilution titers in the dye test in each of the twins and in the mother. In neither case has there been any evidence of intracerebral deposits of calcium. Two younger siblings have shown no clinical or serological evidence of toxoplasmosis.

# Abstracts from Current Literature

## Metabolism; Infant Feeding; Milk and Other Foods

DISORDERS OF GLYCOGEN METABOLISM, WITH SPECIAL REFERENCE TO GLYCOGEN STORAGE DISEASE AND GALACTOSEMIA. WILLIAM H. LANGWISCH and JOHN A. BIGLER, Pediatrics **9**:263 (March) 1952.

Five cases have been presented with evidence of disordered glycogen metabolism. Two cases of glycogen-storage disease of the liver are included, which were confirmed by biopsy, together with clinical and laboratory evidence. Treatment of one of the patients with corticotropin resulted in a disappearance of hypoglycemia and acetonuria during the period of therapy.

Two cases of glycogen-storage disease of the heart are reported, together with clinical histories and necropsy reports. An electrocardiogram which was recorded on one of the patients is included. A case of galactosemia is reported, together with extensive laboratory evidence of marked galactose intolerance.

The criteria for the diagnosis of these entities are reviewed and the symptomatology, physical findings, treatment, prognosis, and pathologic manifestations are discussed.

FROM THE AUTHORS' SUMMARY.

## Vitamins; Avitaminoses

VITAMIN-RESISTANT RICKETS. LUIS GIVOVICH, Rev. chilena pediat. **21**:81 (Feb.) 1950.

The author reports the clinical history of an infant with vitamin-resistant rickets. The infant was born after a normal pregnancy, breast fed until he was 4 months old, and given adequate amounts of vitamin D from the age of 2 months. At the age of 3 months the diagnosis of rickets was established, and the child received a single dose of 600,000 units of vitamin D by mouth. Because clinical and laboratory signs of rickets still persisted he received during the following months a total of 6,000,000 units of vitamin D injected in 10 massive doses. The infant died of pneumonia at the age of 9 months, and, at autopsy, findings of characteristic rickets were observed. The endocrine glands were normal.

The author reviews the literature and analyzes the different types of rickets.

FROM THE AUTHOR'S SUMMARY.

VARIATIONS OF VITAMIN H LEVEL IN MOTHER'S MILK DURING A PERIOD OF 12 MONTHS (SEPTEMBER, 1948, TO AUGUST, 1949). J. HOMOLKA and J. RIMAN, Paediat. danub. **6**:181 (Oct.-Dec.) 1949.

The maximum and the minimum biotin (vitamin H) levels in mother's milk occur in certain months. In months with a low concentration of biotin in mother's milk, the incidence of Leiner's disease (desquamative erythroderma) increases. Only in special cases of biotin deficiency in mother's milk can the level of vitamin H be raised by administration of biotin in chocolate.

FROM THE AUTHORS' SUMMARY.

## Newborn

ERYTHROBLASTOSIS FETALIS. SHINOUDA, J. Roy. Egyptian M. A. **34**:240, 1951.

This is a general discussion of the subject of erythroblastosis fetalis. It contributes nothing new.

McGUIGAN, Evanston, Ill.

## Acute Infectious Diseases

ORAL PENICILLIN IN THE PROPHYLAXIS OF RECURRENT RHEUMATIC FEVER. MARTIN M. MALINGER, J. Pediat. **37**:858 (Dec.) 1950.

Streptococcus hemolyticus was temporarily removed from the throats of rheumatic children by the use of 5,000-unit penicillin throat troches. The author prescribes the use of three such troches daily from September through June.

TREATMENT OF TYPHOID FEVER WITH TERRAMYCIN. WILLIAM A. REILLY and A. M. EARLE, J. Pediat. **38**:428 (April) 1951.

The authors treated six typhoid patients with terramycin and found the drug effective in four of them. Failure of the other two to respond to treatment may have been because the dosage was too small. The authors suggest doses of 100 to 200 mg. per kilogram per day for the treatment of typhoid. The higher dosage should be used in severe cases.

MACDONALD, Pittsburgh.

DECLINE IN MORTALITY IN ACUTE RHEUMATIC FEVER IN NEW HAVEN, CONN., 1920-1948. ROBERT W. QUINN and JULIA P. QUINN, New England J. Med. **245**:211 (Aug. 9) 1951.

From 1920 to 1948, there were 1,144 deaths resulting from rheumatic heart disease and its complications in New Haven, Conn. Among persons from 2 to 24 years old, a steady decline in mortality was noted, whereas among persons older than 24 years, the rate of death from the same cause was unchanged. The authors speculate that this situation results from the decreased prevalence of rheumatic fever in New England, which in turn may be the consequence of better housing conditions and, hence, fewer exposures to beta hemolytic Streptococcus infections. It is well known, further, that one expression of streptococcosis, viz., scarlet fever, is decidedly less virulent and less common; and this may be true of other forms of beta streptococci.

WHEELOCK, Denver.

TERRAMYCIN IN TREATMENT OF SALMONELLA CHOLERAESUIS BACTEREMIA. R. B. SCOTT and C. H. WOODING JR., Pediatrics **7**:349 (March) 1951.

Terramycin is an antibiotic derived from the soil actinomycete, Streptomyces rimosus. It inhibits a wide variety of bacteria, including Gram-negative bacilli. At present only the oral route of administration is recommended. This report deals with the use of terramycin in children infected with Salmonella choleraesuis. Three small children, complaining of vomiting, fever, anorexia, and diarrhea, were recently treated by the authors. All the children were actually ill and toxic. S. choleraesuis was isolated from the blood stream in each case. These children were treated with terramycin hydrochloride in dosage of 2 to 3 gm. daily.

Encouraging results were obtained in all cases. The average duration of toxicity and temperature (above 37.2 C. [99.0 F.] rectally) was approximately five days after administration of the antibiotic. Blood cultures became negative within 48 days in two children and after five days in the other. No untoward reactions were observed. The drug was readily accepted when administered orally. Though appraisal of the therapeutic effect of terramycin is difficult because of the variability of duration of the untreated disease, it would appear that terramycin may be superior to the sulfonamides and to other currently available antibiotics in the treatment of S. choleraesuis septicemia in children.

FROM THE AUTHORS' SUMMARY.

DIPLOCOCCUS CRASSUS SEPTICEMIA. H. M. CARDULLO, I. SCHULMAN, and FRANCES CAPRON SMITH, Pediatrics **7**:355 (March) 1951.

Diplococcus crassus is a common inhabitant of the normal nasopharynx and is ordinarily of low pathogenicity. At times, however, it may assume marked virulence, and in the European literature may be found numerous reports of meningitis and septicemia, as well as reports of more isolated cases of pneumonia, otitis, mastoiditis, lymphadenitis, cerebral abscess, tonsillitis, purpura, and pyelocystitis due to this organism. The outstanding bacteriologic characteristic of D. crassus is that it may be either Gram-positive or Gram-negative, and often both staining reactions may be seen in smears made from the same colony. This paper reports a case of D. crassus septicemia in a premature infant, characterized by sudden onset and marked lymph-node involvement, with recovery following the use of combined chemotherapy.

FROM THE AUTHORS' SUMMARY.

RECOVERY OF SPIRILLUM FROM 2 CHILDREN WITH FEVERS. G. SHWARTZMAN, A. L. FLORMAN, M. H. BASS, S. KARELITZ, and DOROTHEA RICHTBERG, Pediatrics **8**:227 (Aug.) 1951.

A Spirillum was repeatedly recovered by blood culture from two children. This organism resembled the Spirillum minus which has long been associated with one form of rat-bite fever, sodoku. In sodoku the Spirillum is usually recovered by animal inoculation, and no previous record has been found in which a diagnosis has been made by blood culture.

The organisms recovered from the two patients were morphologically indistinguishable from the classic Spirillum minus, but they were unique in that they could be maintained for many months on standard liquid and solid bacteriologic media. Their in vivo resistance to penicillin and arsenicals was very marked and therefore also unusual. Both patients suffered from recurrent fever, eruption, and symptoms referable to the central nervous system and the respiratory and intestinal tracts. One child died, having failed to respond to arsenicals, penicillin, and streptomycin. In the second child, the use of aureomycin was finally successful in sterilizing the blood stream and healing the ulcers after a prolonged course.

FROM THE AUTHORS' SUMMARY.

TREATMENT OF SHIGELLA INFECTION WITH POLYMYXINS. D. LIEBERMAN and E. JAWETZ, Pediatrics **8**:249 (Aug.) 1951.

In acute bacillary dysentery many chemotherapeutic agents can alleviate the symptoms and suppress the infecting organisms. In an institution for mentally defective children, 93% of 116 patients with fresh infection with Shigella responded to therapy with sulfonamides, or other antimicrobial agents, but only 63% of 78 chronically infected patients responded.

The control of shigellosis in an institution depends largely on the eradication of carriers and other chronic "shedders." Conventional chemotherapy is not highly efficacious in such patients. Polymyxin, a stable polypeptide from Bacillus polymyxa, is strongly bactericidal for Shigella. This drug is not absorbed from the intestinal tract when administered orally. Twenty-three children with chronic intestinal infections with Shigella paradysenteriae (Flexner) received polymyxin, in a dosage of 15 to 20 mg. per kilogram by mouth daily for 10 days. Twenty (87%) were unequivocally cured of the infection which previously had resisted all other treatment. No toxic effects were observed. Polymyxin appears to be a useful drug for the oral treatment of patients with chronic Shigella infection.

FROM THE AUTHORS' SUMMARY.

CANICOLA FEVER. ALEXANDER JOE and GEORGE SANGSTER, Edinburgh M. J. **58**:140 (March) 1951.

Leptospira canicola is widely distributed among dogs in the United Kingdom. It is assumed that the infection in man is acquired from infected dogs by way of contact or broken skin, mucous membranes, upper respiratory passages, or the conjunctiva. The disease in humans is benign. Involvement of the meninges is the common presenting feature. Diagnosis is made by isolation of L. canicola from the blood or urine or by the demonstration of specific antibodies in the patient's serum. The authors present three cases in which the patients recovered.

MACDONALD, Pittsburgh.

SULPHABENZAMINE, A DRUG FOR BACILLARY DYSENTERY. U. P. BASU, and A. N. BOSE, J. Indian M. A. **20**:312 (June) 1951.

The results of pharmacological, chemical, and clinical studies are presented regarding sulfabenzamine, a new sulfonamide compound used for the treatment of bacillary dysentery. The drug appears to be well tolerated, of very low toxicity, and highly effective in bacillary dysentery.

MCGUIGAN, Evanston, Ill.

CHLOROMYCETIN AS A THERAPEUTIC AGENT IN TYPHOID AND PARATYPHOID IN CHILDREN. F. HATZ, Ann. pædiat. **175**:121 (July-Aug.) 1950.

In one case of typhoid and four cases of paratyphoid B in children, aged 1¾ to 12 years, a favorable influence of chloramphenicol (chloromycetin®) on the course of the illness was found. However, the development of a periarthritic focus in a boy of 2¾ years with paratyphoid B was not prevented by chloramphenicol. FROM THE AUTHOR'S SUMMARY.

"IRGAPYRIN" AS AN ANTIRHEUMATIC. WALTER BELART, Schweiz. med. Wchnschr. **79**:582 (June 25) 1949.

"Irgapyrin," a pyrazolidin derivative, has been used clinically in treatment of patients with certain forms of arthritis, arthrosis, lumbago, brachialgia and tendinitis. Against infectious arthritis and polyarthritic exacerbations good results were obtained often. The drug is given slowly, intragluteally or, rarely, intravenously, in a dosage of 5 cc. in 30% solution at intervals of one to two days. Usually four to five injections were given. No disagreeable side-effects were noted, even upon longer application, with the exceptien of occasional pain upon injection and rare erythemas. AMBERG, Rochester, Minn.

DEVELOPMENT OF "EGRESSIN," AN OXYURIS REMEDY. O. ZIMA, F. V. WERDER, A. VAN SCHOOR, A. HOFFMANN, and L. HEPDING, Schweiz. med. Wchnschr. **80**:734 (July 15) 1950.

A large number of urethan derivatives were tested for their action on Oxyuris infection. Of these, N-isoamylcarbamic acid-3-methyl-6-isopropylphenyl ester (preparation No. 130, called "egressin") approached very closely the ideal demands for a remedy against Oxyuris infection in man. It is a crystalline substance, easily soluble in organic solvents but less than 1:50,000 in water. AMBERG, Rochester, Minn.

CLINICAL EVALUATION OF EGRESSIN. SAUER and WEISSFLUG, Schweiz. med. Wchnschr. **80**:737 (July 15) 1950.

It is recommended that children from 2 to 12 years old be given, for two days three times a day, 1 gm. of "egressin" (N-isoamylcarbamic acid-3-methyl-6 isopropylphenyl ester) and that older patients be given 2 gm. three times a day by mouth. The third day a laxative should be given but no castor oil. Thirteen children and 11 adults were treated. Ninety-five per cent of the patients became free from Enterobius eggs for 3 to 8 weeks. The itching disappeared in all cases after three doses. In about one-third of the cases eggs were found again after 4 to 6 weeks. Fifty-seven per cent of the patients remained free of eggs for as long as four months, but 10% proved refractory to the treatment even upon repetition. Beneficial results are mentioned as being obtained in 200 cases of chronic infection. AMBERG, Rochester, Minn.

OXYURICIDAL ACTION OF PHENOLTHIAZINE. A. FORTUNATO and O. JABOLI, Clin. pediat. **33**:51 (Jan.) 1951.

Thiodiphenylamine, administered with a small nonlaxative dose of phenolphthalein, proved to be a very successful drug in overcoming Oxyuris infestation. Good results were obtained in 42 out of 50 patients (mostly children) treated. HIGGINS, Boston.

USE OF GLUCANTIME IN KALA-AZAR IN CHILDREN. I. V. TONDI and F. RIPA, Minerva pediat. **3**:184 (March) 1951.

Two children, aged 7 and 4 years, with kala-azar were treated with very satisfactory results with a pentavalent antimony preparation, "glucantime" (N-methylglucamine antimonate), also called "2.168 R.P." HIGGINS, Boston.

AMOUNT OF ACTIVE COMPLEMENT IN SERA OF TYPHOID PATIENTS, AS AFFECTED BY INTRAVENOUS VACCINE. F. MULÈ and L. GARUFI, Pediatria **58**:893 (Nov.) 1950.

The complement in the sera of patients with typhoid was increased following the injection of typhoid vaccine intravenously. HIGGINS, Boston.

EFFECT OF INJECTIONS OF ADRENAL STEROIDS ON THE ACTIVE COMPLEMENT OF THE BLOOD OF PATIENTS CONVALESCING FROM TYPHOID. F. MULÈ and L. GARUFI, Pediatria **59**:69 (Jan.) 1951.

The active complement in the blood was found to be increased following the injection of whole extract of adrenal gland ("cortigen") and increased to a somewhat lesser degree following injection of synthetic steroids (percorten®). The maximum rise occurred in two hours.

HIGGINS, Boston.

OSTEOPERIOSTITIS IN SODOKU (RAT-BITE FEVER). T. PORCELLI, Pediatria **59**:376 (May) 1951.

Seven days after a 10-month-old baby had been bitten by a rat, there was swelling of the index finger and a high fever. A roentgenogram showed periostitis of the proximal phalanx of the finger. Treatment was by arsphenamine. About three months later, another roentgenogram was made and showed complete recovery of the lesion.

HIGGINS, Boston.

USE OF CHLOROMYCETIN IN CHILDREN WITH TYPHOID: FIFTY-SIX CASES. SALVADOR MARINA, Acta pediat. españ. **9**:462 (April) 1951.

Report is made of a detailed study of 56 children with typhoid, between the ages of 1 and 15 years. Due to water contamination, in all cases the disease developed within a month or two. The water supply having been good previously, none of these children had had any immunization. Because of the presence of an epidemic, medication was started on a clinical basis and was later confirmed by blood cultures, agglutination tests, etc., except in a few cases which occurred before the water supply was found to be contaminated. All patients were treated with chloramphenicol (chloromycetin®), and most of them were kept at home rather than hospitalized.

There were no deaths, no sequelae, and no relapses. Chloramphenicol was administered by mouth in most cases, although a few patients required rectal administration. Unlike the practice in treating adults, an initial massive dose was unneccesary. Fifty milligrams per kilogram of body weight per 24 hours was administered until the fever abated, and for a week longer 25 mg. per kilogram per 24 hours was used. The total dosage was divided into four or six doses. After a week in which no antibiotic was given, 25 mg. was repeated if it was found necessary.

Sufficient calories in a soft diet, which included fruit juices, puréed vegetables, milk, soups, and amino acids, were essential. Ascorbic acid, vitamin K, and liver extract were also administered. All patients had bed rest for at least one month. A detailed chart of information regarding age, sex, symptoms, amounts of chloramphenicol used, etc., is included.

ALLEN, Santa Fe, N. M.

RHEUMATIC DISEASE IN A BABY OF 2½ YEARS. JULIO GUASCH and JULIO ESPINOZA, Rev. chilena pediat. **22**:206 (May) 1951.

The literature on rheumatic fever in children under 3 years old is reviewed, and the authors stress the scarcity of reports. They present the case of a 2½-year-old child who evidenced heart failure with auscultatory signs of mitral insufficiency, and who at autopsy showed rheumatic carditis.

FROM THE AUTHORS' SUMMARY.

CHLOROMYCETIN IN TYPHOID. PEDRO DANIEL MARTINEZ, FERNANDO MADERO, and JULIO M. TORROELLA, Bol. méd. Hosp. inf., México **7**:346 (June) 1950.

The authors present clinical observations gathered at the Hospital Infantil on a series of 50 patients with typhoid, 20 of whom, with positive blood cultures, received the routine hospital care, and 30 of whom (18 with positive blood cultures) received in addition chloramphenciol (chloromycetin®) by mouth, with 50 mg. per kilogram of body weight as the initial dose, and the same amount in 24 hours divided in equal doses every two to three hours for periods ranging from 2 to 14 days. Both groups are analyzed in regard to sex and age distribution, time of evolution at the beginning of the study, and length of time of observation after recovery. All cases occurred in the Federal District from June to October, 1949. Seventy-six per cent of

the patients were controlled personally by one of us (P. D. M.), and the selection of those to receive the drug was determined by the parents' economic ability to acquire the medication.

None of the patients presented any complication or intercurrent disease caused by infectious agents other than Salmonella typhosa, either at the beginning of treatment or during hospitalization. The average duration of fever was the same in both groups (25 days), but continuous fever lasted only 19.8 days in treated patients and 25 days in the untreated. It was seen that patients treated longer than five days were febrile less than five days, with three exceptions; on the other hand, untreated patients were febrile for longer periods, except in two cases. Five patients were found who had positive blood cultures during or after treatment with chloramphenicol, and nine remained as convalescent carriers. No clear action of the drug was observed on the blood picture, the agglutination titers, or the blood pressure. In the majority of patients improvement in general condition was noted, but there were a few variations in local manifestations. In neither group were there any serious complications attributable to associated infections. There were three relapses in the treated patients (one with enterorrhagia), as compared with only one in the untreated. There were no deaths.

Chloramphenicol, in the dosage used, for short periods of time (in 18 cases, from 5 to 14 days, and in 12, less than 5 days), and given late (all after the first week), apparently was able to stop the usual continuous fever of the infections, but it did not impede the presentation of new febrile situations, which were classified generally as of low intensity and intermittent, without any attack on the general condition. Also, the drug did not prevent clinical relapses.

FROM THE AUTHORS' SUMMARY.

OBSERVATION AT HOSPITAL INFANTIL, MEXICO, ON USE OF CHLOROMYCETIN AND AUREOMYCIN IN TREATMENT OF TYPHOID. PEDRO DANIEL MARTINEZ, Bol. méd. Hosp. inf., México **7**:521 (Aug.) 1950.

The author presents the cases of 31 patients with typhoid treated with chloramphenicol (chloromycetin®) and 13 treated with aureomycin. Of the former, 19 had positive blood cultures, and of the latter, 7 had positive blood cultures. Those treated with chloramphenicol received the drug for variable periods, in a dosage of 50 mg. per kilogram of body weight as the initial dose, followed by the same amount divided into eight equal doses in 24 hours. The patients treated with aureomycin all received the medication for 10 days in a dosage of 50 mg. per kilogram of body weight.

A comparison was made between the two groups and a control group of 20 patients all of whom had positive blood cultures. The following results of this study are of interest. Of 19 children treated with chloramphenicol for over five days, only 3 continued to have fever for more than five days; on the other hand, in those who received the drug for a shorter period of time, no apparent modification in the usual febrile course was observed. In the patients treated with chloramphenicol, frequent febrile relapses were seen; and 6 of the 19 patients with positive blood cultures remained positive during or after a one-to-three-day treatment. Ten convalescent carriers were found in this group. On the other hand, the cases treated with aureomycin were apparently not affected by the use of the drug. No intolerance to the medication was observed.

FROM THE AUTHOR'S SUMMARY.

CHLOROMYCETIN TREATMENT OF SALMONELLA INFECTIONS. P. CHRIST, Deutsche med. Wchnschr. **76**:772 (June 8) 1951.

Ten adults with Salmonella infections were treated with chloramphenicol (chloromycetin®). In five of seven patients with typhoid treated during the second and third week, a definite beneficial effect became manifest. A patient with paratyphoid-B infection was also benefited. Two patients with severe gastroenteritis due to Salmonella infections did not respond. A paratyphoid carrier also did not respond, nor did a typhoid carrier whose treatment was perhaps too short.

AMBERG, Rochester, Minn.

NEW TREATMENT OF TYPHOID AND PARATYPHOID. EUGEN SCHLIEF and HANS SCHLIEF, Med. Klin. **44**:867 (July 8) 1949.

A new preparation is recommended for the treatment of typhoid and paratyphoid. The authors used it in treatment of about 60 patients during a period of about 18 years. The preparation, "neo-ballistol," is composed of liquid petrolatum, alkali salts of oleic acid, ammonia, and a small amount of 2 methyl-4 butanol, 2 methyl-1 propanol, and peppermint oil. It is strongly bactericidal for various pathogens and is administered by mouth.

TREATMENT OF CHRONIC PURULENT PROCESSES WITH FERMENT "P.Z.44." HELLMUTH WILL, Med. Klin. **46**:868 (Aug. 10) 1951.

Ferment "P.Z. 44" is a proteolytic ferment. It acts like kathepsin occurring in leucocytes. It liquefies necrotic material and so renders wounds clean. It is not irritating or only slightly so. It is used in cases of bacterial infection in addition to antibacterial therapy.

AMBERG, Rochester, Minn.

AIRBORNE INFECTIONS: IV. CONTROL OF DUST-BORNE STREPTOCOCCIC INFECTIONS IN CHILDREN'S WARDS. GUNNAR LAURELL, Acta pædiat. **37**:237, 1949.

An investigation into the control of dust-borne hemolytic streptococci was carried out in two identical children's wards during the autumn of 1946 and the spring of 1947. In one, the oiled ward, all the bedclothes and ward linen were treated in the hospital laundry with triton oil, and the floor of the ward unit was oiled. In the unoiled ward no antidust measures were taken.

The investigation showed that (1) the number of nosocomial infections was not affected by the steps taken; (2) the presence of a dangerous carrier was of decisive importance in accounting for nosocomial infections, and (3) consequently, in judging the value of prophylactic measures, no conclusion could be drawn without consideration of the decisive importance of dangerous carriers.

FROM THE AUTHOR'S SUMMARY.

RHEUMATIC PNEUMONIA. HARALD OLESEN, Ugesk. læger **112**:758 (May 25) 1950.

Two cases are reported of rheumatic pneumonitis in boys 16 and 7 years old who died from typical rheumatic pancarditis. The postmortem examination of the first patient disclosed marked fibrinous hemorrhagic alveolitis in the lungs, with scanty necrotic vascular lesions, and in the second patient, focal fibrinous necrosis of the alveolar walls and fibrinous and hyaline thrombosis of the capillaries with exudative lesions. The author discusses the pathogenesis and is of the opinion that the lesions should be considered a pulmonary manifestation of the allergic rheumatic reaction.

WALLGREN, Stockholm, Sweden.

NOSOCOMIAL STREPTOCOCCIC INFECTIONS IN A CHILDREN'S INSTITUTION. SVEN HELBO, Ugesk. læger **112**:823 (June 8) 1950.

The author discusses the nosocomial spread of streptococci among the personnel and children in a seashore hospital. The penicillin treatment is effective but deprives the children of immunity. This may lead to reinfection. Penicillin treatment may also lead to development of more virulent dominating streptococci. It is recommended that penicillin be used only when the streptococci have produced suppurative complications.

WALLGREN, Stockholm, Sweden.

A CASE OF ORNITHOSIS. H. PRAKKEN, Maandschr. kindergeneesk. **18**:341, 1950.

A 3½-year-old girl became ill with fever and abdominal pain. Pleural exudate was found, from which no bacteria could be cultured. The guinea-pig test revealed no bacteria. Penicillin was administered. Later it was found that the father possessed carrier pigeons. On the 65th day of the disease the complement fixation test with psittacosis virus was positive. Isolation of the virus at that stage was not possible. The author concludes that administration of penicillin inhibits a further rise of the antibody content of the serum.

VAN CREVELD, Amsterdam, Netherlands.

EXPERIENCES WITH CHLOROMYCETIN. F. VAN GELDEREN, Maandschr. kindergeneesk. **19**:172 (July) 1951.

A report is given on the clinical use of chloramphenicol (chloromycetin®) for 13 children with paratyphoid and typhoid and for 15 children with whooping cough. The results in the children with paratyphoid were striking, constant, and nontoxic, with no relapses. In the child with typhoid there was a relapse which was quickly and completely overcome. The effect of chloramphenicol in 15 children with whooping cough, with special regard to the number of severe coughing attacks as compared with the number in 15 controls, was disappointing.

FROM THE AUTHOR'S SUMMARY.

FREQUENCY OF RELAPSE OF TYPHOID IN PREWAR PERIOD AND DURING THE WAR IN ALMA-ATA, KAZAKHSTAN. O. A. LYCENKO, Pediatriya **2**:63 (March-April) 1951.

It is reported by the author that the frequency of relapse in typhoid patients in Kazakhstan, U. S. S. R., was higher during the war and sometimes recurred two or more times. The majority of recurrent attacks were among children 6 to 10 years old, and relapses occurred most frequently during the height of an epidemic. Relapse is more frequently characterized by subfebrile temperature, with temperature occasionally rising to 38 C. (100.4 F.). The duration of relapse is much shorter than in the original illness.

The marked frequency of relapse during the war, the author states, is due to immunobiological changes of the entire organism in changed living conditions. In the majority of cases preliminary symptoms were absent. A few cases were marked by general apathy, lack of appetite, and absence of splenic and liver contractions. All the symptoms of typhoid returned, however, as the relapse progressed, except that roseola was less marked and appeared earlier. In 26.9% of cases of relapse rose spots were absent. The recurrent illness is usually a light form; no mortality was noted. There were no complications in prewar cases. In wartime cases there were a few occurrences of cardiac failure and colitis and one instance of gastrointestinal disturbance.

BODER, Los Angeles.

"PENTOSTAM" IN FIELD TREATMENT OF KALA-AZAR. C. JUNG SUN, Chinese M. J. **67**:184 (April) 1949.

"Pentostam," containing 100 mg. of pentavalent antimony per cubic centimeter, was used in treatment of 510 patients with kala-azar. The results indicate that of the pentavalent antimony compounds available, "pentostam" is the least toxic and the best tolerated. The recovery rate is high.

MACDONALD, Pittsburgh.

SALMONELLA INFECTIONS IN INFANCY AND CHILDHOOD. S. Y. CHANG, J. FOURNIER, and C. SUNG, Chinese M. J. **67**:291 (June) 1949.

The authors report 36 cases of Salmonella infections in infants and children. Nine cases of paratyphoid A were seen in older children. The organism is endemic in Shanghai throughout the year. Nineteen cases of paratyphoid B, 15 of these in infants, are reported, all occurring in the summer months. In addition, cases infected with Salmonella typhimurium, Salmonella derby, Salmonella anatis, Salmonella aberdeen and Salmonella of the C type were seen. Fever and diarrhea were the main symptoms. Treatment was with sulfonamides, penicillin, or streptomycin. One patient (S. anatis) died. The others recovered, and these had no relapses.

MACDONALD, Pittsburgh.

## Chronic Infectious Diseases

EFFECT OF ANTIHISTAMINIC DRUGS UPON THE TUBERCULIN REACTION. MILTON GRAUB, and ELLIS M. BARRIST, Am. Rev. Tuberc. **61**:735 (May) 1950.

A group of 95 patients with exudative or productive tuberculosis were given a control tuberculin test with 0.1 cc. of PPD (purified protein derivative). The reaction was positive in all patients. A week later 50 mg. of diphenhydramine (benadryl®) hydrochloride was administered every four hours. On the second day of treatment another test was made using 0.1 cc.

of PPD, and readings were taken 48 hours later. All readings were based on the size of the area of induration. Seventy-three per cent of the 95 patients showed depression of the tuberculin following the administration of therapeutic doses of diphenhydramine or pyrilamine (neoantergan®) maleate. The results were the same in patients with exudative tuberculosis and in those with productive tuberculosis.

Tuberculin skin tests should not be attempted when antihistaminic drugs are being administered.

EUGENE SMITH, Ogden, Utah.

THE LOCAL EFFECT OF CORTISONE ON THE TUBERCULIN REACTION. HERMANN VOLLMER, J. Pediat. **37**:22 (July) 1951.

Systemic treatment with corticotropin (ACTH) or cortisone will temporarily suppress the tuberculin reaction. It appears, from Vollmer's experiments, that this effect is produced by a certain cortisone concentration in the skin and not through mediation of other mechanisms affected by these hormones.

When a mixture of cortisone and old tuberculin is injected into the skin of tuberculin-sensitive patients, the tuberculin reaction is diminished. Corticotropin used locally does not alter the tuberculin reaction. Local tissue reaction to the cortisone-tuberculin mixture showed a relative decrease of lymphocytes, as compared with the reaction to tuberculin alone. In addition, the tuberculin-cortisone mixture was less pruritic.

Vollmer also noted that local cortisone can suppress skin reactions to diphtheria toxin. "Rebound" reactions were seen in patients tested with cortisone-tuberculin mixtures and with cortisone plus diphtheria toxin. They occurred after the fifth day. They were thought to be the result of temporary suppression of skin sensitivity. The tuberculin or diphtheria toxin lay dormant in the skin. When the cortisone was absorbed, the testing material elicited a reaction.

Vollmer thinks that, since cortisone used locally decreases tissue response in general, it may possibly help in the treatment of eczema. Whether there is additional interference with the antigen-antibody reaction in the tuberculin test, remains to be seen.

MACDONALD, Pittsburgh.

RESULTS OF HISTOPLASMIN SKIN TESTING IN CHILDREN FROM THE ST. LOUIS, MO., AREA. JOHN F. LYNCH and E. BRYCE ALPERN, M.D., J. Pediat. **38**:51 (Jan.) 1951.

Five hundred infants and children admitted to St. Louis Children's Hospital were tested with histoplasmin. Seventy-three (14.6%) had positive reactions. This figure, which is lower than some previous reports from Missouri, is explained by the fact that about one-half the children in the present report were under 3 years old. The results of this study indicate that positive reactions to histoplasmin increase rapidly in incidence up to 10 years. Most of the positive reactors came from rural communities. Boys were affected more frequently than girls. Although none of the positive reactors had evidence of active histoplasmosis, most of them had some sort of chronic illness. All the positive reactors under 3 years old showed signs of some chronic disease. None of these were tuberculin-positive.

MACDONALD, Pittsburgh.

BCG TUBERCULIN AS A TESTING MATERIAL. ELI FRIEDMAN and IRVING SILVERMAN, New England J. Med. **241**:894 (Dec. 8) 1949.

When the strength of old tuberculin (OT) or purified protein derivative (PPD) is increased during diagnostic testing, both the frequency of pseudoreactions and the likelihood of severe positive reaction increase. The authors tested 91 children with, a 1 : 10,000 dilution of BCG tuberculin and OT simultaneously, and compared the results from both the above points of view. Methods of testing and critical evaluation were identical.

Finally, 10 known positive reactors were tested consecutively with a 1 : 100 dilution of OT and a 1 : 100 dilution of BCG. The preliminary conclusions reached were that BCG tuberculin is a safe and reliable testing material and that fewer pseudoreactions and less severe local and general reactions occur with its use. Alternative explanations for the difference in reactions between BCG tuberculin and existing products are given.

WHEELOCK, Denver.

THE USE OF BCG. ARMAND FRAPPIER and ROLAND GUY, Canad. M. A. J. **61**:18 (July) 1949.

A program for extensive use of BCG vaccine in the province of Quebec is outlined, with a discussion of the preferred technique of vaccination and results obtained in other similar programs. Vaccination with BCG is being integrated into the program of tuberculosis control in Quebec.

McGUIGAN, Evanston, Ill.

ALLERGOMETRY IN TOXOPLASMOSIS. O. THALHAMMER and L. JANICEK, Ann. pædiat. **177**:116 (Aug.) 1951.

By using allergometry as a test, an attempt has been made to distinguish between patients suffering from toxoplasmosis and healthy carriers. It has been found that of 100 persons who were toxoplasmin-positive, only 11 had a pleo-esthetic reaction; of these 63.6% showed suggestive symptoms. Among 31 homodynamic persons, this was the case in 12.9%; among 58 pleo-ergic persons, in 8.6%, i. e., just as often as among the 59 persons who were toxoplasmin-negative (19.1%) during the period under investigation. Allergometry thus appears to be justified as a means of discriminating between affected persons and carriers who should be followed up.

FROM THE AUTHORS' SUMMARY.

TREATMENT OF SYPHILIS IN MOTHER AND CHILD AND ITS RESULTS. J. B. MAYER and H. F. HERKENHOFF, Ann. pædiat. **177**:194 (Oct.) 1951.

As a result of observations on 151 children with congenital syphilis during 1945 and 1950, the authors investigated syphilitic infections in the mothers, 70 of whom were found to be unaware of the infection. Thirty-six mothers had been treated for syphilis during pregnancy. The Wassermann reaction was negative in 12 mothers and their children, but in 6 of these children there were definite signs of the illness.

The authors attempt to show the advantages of pencillin treatment over acetarsone (stovarsol®) for syphilitic children. The law of Farmer and Gyorgy, which states that the Jarisch-Herxheimer reaction is an "all or nothing" law, is not accepted. Large doses of penicillin cause a severe Jarisch-Herxheimer reaction; small doses, a reaction of medium strength, and very small doses, a slight reaction. A scheme is given for the treatment of syphilitic children.

FROM THE AUTHORS' SUMMARY.

MEDIASTINAL AND SUPRACLAVICULAR COLD ABSCESS FROM HILUS TUBERCULOSIS. W. FRISCHKNECHT, Helvet. pædiat. acta **5**:472 (Nov.) 1950.

The author describes a rare complication which developed in a child suffering from tuberculosis of the paratracheal lymph nodes. In a 6-year-old boy round bilateral, supraclavicular swellings, which were tense and fluctuating, suddenly appeared. Clinical, roentgenological, bacteriological, and histological investigations revealed that there was a tuberculous cold abscess of the upper posterior mediastinum and of the supraclavicular region. This communicating abscess healed within two months after surgical drainage of the left supraclavicular cavity, regular irrigations with 2% paraaminosalicylic acid, and intramuscular injection of streptomycin.

FROM THE AUTHOR'S SUMMARY.

RHESUS GENOTYPE DIVISION AMONG THE PEOPLE OF EASTERN SWITZERLAND. L. HOLLANDER, Helvet. pædiat. acta **6**:255 (June) 1951.

The distribution of Rh types among the population in northeastern Switzerland is reported upon, and an analysis of the data on 400 persons is given.

GRULEE, Evanston, Ill.

CHEMOTHERAPY OF TUBERCULOSIS WITH PARA-AMINOSALICYLIC ACID: PARA-AMINOSALICYLIC ACID PREPARED ACCORDING TO A NEW SYNTHETIC PROCEDURE ("AMINACYL," WANDER). H. STEINLIN and E. WILHELMI, Schweiz. med. Wchnschr. **78**:1219 (Dec. 18) 1948.

The results of treatment of 106 patients with tuberculosis with "aminacyl" (a synthetic preparation of paraaminosalicylic acid) are discussed. The drug was administered orally in 53 cases, locally in 37, and by a combination of methods in 16 cases. It was found advantageous

to use dragées of the sodium salt for oral administration, each containing 0.34 gm., corresponding to 0.3 gm. of the free acid. Usually 10 dragées were given four times a day, that is, 12 gm. of free acid for four consecutive days. Then administration was suspended for three days. In treatment of renal tuberculosis, 6 to 9 gm. of free acid could be given daily for six to eight weeks, with a pause of 8 to 14 days. The cure should be extended over a period of at least four to six months. Blood concentrations were measured repeatedly. Generally the concentrations varied between 2 and 16 mg. per 100 cc., and after the 12-hour night interval it often was 0.5 to 2.5 mg. per 100 cc. Daily maxima were found in the late afternoon. In a few cases, a combination treatment with streptomycin was of benefit. Local application was used in pleural empyema and exudates, cavities, following thoracocautery as prophylactic measures, in fistulas, tuberculous lymphomas, and skin tuberculosis. A definite therapeutic effect was noticeable. In a large percentage of cases a beneficial effect manifested itself in reduction of fever, sedimentation rate, cough, expectoration, and bacilli in the sputum. Even more regular and usually more intense was the influence on the general health, appetite, body weight, and hemoglobin content of the blood.

AMBERG, Rochester, Minn.

AUTOMATIC, ENDOGENOUS LYMPHADENOBRONCHOGENIC REINFECTION IN THE INITIAL PERIOD OF PHTHISIS OF THE LUNGS AND ITS TYPICAL CONSEQUENCES. P. SCHWARTZ, Schweiz. med. Wchnschr. **79**:467 (May 21) 1949.

The author emphasizes the fact that reinfection, through a breakdown of a lymph node in the lungs, can occur four to six weeks after a primary infection. As an illustration, the case is cited of an infant who died at the age of 2 months due to an automatic endogenous lymphadenobronchogenous reinfection. The mother had tuberculosis, and it is assumed that the infant was infected at birth or in the first days of life. Primary foci in the lungs at the height of their development were represented by infiltrations, the largest of which were the size of a cherry, but these may become submerged in infiltrations of reinfection.

AMBERG, Rochester, Minn.

STUDY OF FACULTATIVE BCG VACCINATION IN A SCHOOL POPULATION. GEORGES GUYE, Schweiz. med. Wchnschr. **79**:589 (July 2) 1949.

Vaccination with BCG by cutaneous scarification is regarded as the method of choice. The number of cases studied with regard to the incidence of tuberculosis was 292, in 173 of which the patients were tuberculin-anergic.

AMBERG, Rochester, Minn.

OSTEOARTICULAR TUBERCULOSIS IN CHILDREN. P. D. BARIGAZZI and E. OMODEIZORINI, Arch. ital. pediat. e puericolt. **14**:371, 1951.

Report is made of a study of 367 patients with tuberculosis of the bones and joints. The necessity of looking upon the various forms of tuberculosis as a unitary disease, of which the etiologic, the pathogenetic, the prophylactic, and, to a certain extent, the therapeutic problems in the pulmonary and extrapulmonary forms should not be considered isolated, has been confirmed.

FROM THE AUTHORS' SUMMARY.

STREPTOMYCIN IN MILIARY TUBERCULOSIS AND IN OTHER FORMS OF CHILDHOOD TUBERCULOSIS. F. CICCIOLI, Clin. Pediat. **31**:110 (Feb.) 1949.

Clinical cures were obtained in the five children by the use of streptomycin. Four of them had miliary pulmonary involvement, and of these, one also had an exudative process in the bronchi and hilum-gland enlargement. The fifth child was a 3-month-old baby with primary hilum-gland involvement.

HIGGINS, Boston.

ALLERGOMETRY IN CHILDHOOD TUBERCULOSIS. G. LODI, Clin. pediat. **31**:129 (March) 1949.

The degree of sensitivity to tuberculin was determined in 90 children with latent tuberculosis in a sanatorium, and in 90 children with active tuberculosis in a pediatric clinic. The degrees of sensitivity were found to be approximately in the same proportion in the two groups. Anergy to tuberculin was present in each of the three cases of miliary tuberculosis. Of the eight patients

with tuberculous meningitis, one showed anergy, two reacted to a dilution of 1 : 100, three reacted to a dilution of 1 : 1,000 and two reacted to a dilution of 1 : 10,000. All the children with active hilar adenitis, infiltrative pneumonitis, or pleurisy reacted to dilutions of 1 : 10,000, and 50 per cent of them to dilutions as weak as 1 : 1,000,000. The sensitivity was very high in the patients with erythema nodosum; of five patients, three reacted to a dilution of 1 : 1,000,000 and two to a dilution of 1 : 10,000,000.

HIGGINS, Boston.

MULTIPLE CONGENITAL MALFORMATIONS OF THE LEFT HAND IN AN INFANT WITH HEREDITARY SYPHILIS. G. POSTERARO, Lattante **19**:665 (Nov.) 1948.

A 4-month-old baby had hypertrichosis on the back, absence of the left pectoral muscles and left nipple, only two phalanges on each finger of the left hand, and a shortening of the left arm and the left fingers. No scars were noticeable. Both the parents and the infant had positive Wassermann reactions. The mother had had three children and one miscarriage; during her pregnancy she had had irregular treatments for syphilis and periods of marked nausea and vomiting. While one primary cause of the baby's condition, namely syphilis, appears likely, other concomitant factors, such as the postwar poverty and discomfort and the prenatal ill health of the mother, may have played a role.

HIGGINS, Boston.

CONGENITAL SYPHILIS AND PENICILLIN. T. PORCELLI, Lattante **22**:225 (April) 1951.

Seven infants, 2 months old or younger, with congenital syphilis were treated with daily doses of 100,000 to 200,000 units of penicillin. The signs of the disease in the skin, the mucous membranes, the liver, the spleen, and the gastrointestinal tract responded quickly to penicillin treatment; the osseous manifestations were slow to disappear. The serological reactions remained positive for a long time.

HIGGINS, Boston.

PARA-AMINOSALICYLIC ACID IN THE TREATMENT OF TUBERCULOSIS. M. SCARZELLA, Minerva pediat. **1**:79 (Feb.) 1949.

Clinical reports are given regarding 14 patients (8 children and 6 adults) with various types of tuberculosis who were treated with paraaminosalicylic acid. The adults received 12 gm. daily, and the children received up to 6 gm., divided into four doses. This treatment resulted in quick and often dramatic improvement, as shown by general anesthesia, lowered temperature, slower sedimentation rate, increase in weight, and lessening of the cough and expectoration. Excellent results were obtained in primary (childhood) tuberculosis and in pleurisy with effusion; some paraaminosalicylic acid was administered intrapleurally in the latter condition. The anatomic improvement, in patients with tuberculous cavities, as indicated by frequent roentgenograms of the chest, however, was only slight and was far from paralleling the clinical improvement. One child with tuberculosis of the hip was not benefited by paraaminosalicylic acid.

HIGGINS, Boston.

PARA-AMINOSALICYLIC ACID IN TREATMENT OF TUBERCULOSIS. M. SCARZELLA and G. P. SORMANO, Pediatria **56**:645 (Oct.-Dec.) 1948.

The authors report the results obtained with paraaminosalicylic acid aerosols in animals. Following these treatments, hemorrhage and pneumonia have developed. It is believed that these methods of administration of paraaminosalicylic acid in humans are not advisable because of reactions which may occur in tuberculous lungs.

FROM THE AUTHORS' SUMMARY.

CRANIOENCEPHALOGRAPHY IN TREATMENT OF TUBERCULOUS MENINGITIS WITH STREPTOMYCIN. GIULIO MURANO, Pediatria **56**:657 (Oct.-Dec.) 1948.

After a brief report on the peculiarities of the clinical picture and of the pathological alterations observed in patients with tuberculous meningitis treated with streptomycin, the author reports the results of encephalographic research in children with this disease treated with this drug.

He emphasizes the frequency of encephalographic symptoms of intracranial hypertension of the convexity, as well as of the base of the brain, and also the frequency of encephalographic

dilatations of the arachnoid-ventricle system. The last dilatations are more-or-less accentuated and often are not proportional to the various parts of the system (subarachnoid spaces and ventricles). It was possible to observe that the internal and often the external hydrocephalus appears rather early, and obstructions in the various portions of the system were noted often. Such obstructions separate one (or both) lateral ventricles, or sometimes the ventricle system or the whole subarachnoid-ventricle system, from the spinal fluid circulation.

The author stresses the usefulness of encephalographic results in developing the most suitable treatment in each case, and he discusses the eventual advantages or dangers of air injection into the spinal column in tuberculous meningitis. FROM THE AUTHOR'S SUMMARY.

LOCAL INJECTION OF VITAMIN $D_3$, STREPTOMYCIN, AND PARA-AMINOSALICYLIC ACID IN TUBERCULOUS LYMPHADENITIS. G. COCOZZA, Pediatria **57**:521 (July) 1949.

Twenty children with tuberculous adenitis were treated by intraglandular injections of streptomycin (50 to 100 mg. every three days). If the glands had abscessed, the tuberculous pus was first aspirated and the area irrigated with isotonic sodium chloride solution. Very satisfactory results were obtained. Injections of calciferol (vitamin $D_3$) were an efficacious adjunct to streptomycin in the more severe infections; in some cases calciferol injections alone seemed to be of benefit. Intraglandular injections of paraaminosalicylic acid (PAS) proved to be of little or no therapeutic value. HIGGINS, Boston.

AN ENCEPHALOPATHIC REACTION FROM A BURN IN A CHILD WITH ALLERGIC TUBERCULOUS MENINGITIS. G. CROCCO, Pediatria **57**:551 (July) 1949.

A child of 28 months with allergic tuberculous meningitis reacted to a third-degree hot-water-bottle burn with an episode of blindness, deafness, and choreo-athetosis. Recovery followed treatment with streptomycin, adrenal cortex extract, dextrose by hypodermoclysis, and sedatives.

HIGGINS, Boston.

RELATION OF ALLERGIC MANIFESTATIONS OF PRIMARY TUBERCULOSIS TO LATER TUBERCULOUS LESIONS. G. MELI, Pediatria **57**:883 (Nov.) 1949.

The clinical course is outlined in nine cases of primary tuberculosis, in which destructive lesions later developed. The suggestion is made that the lesions of primary tuberculosis are allergic in nature and are necessary in preparing the field for later caseous or destructive lesions.

HIGGINS, Boston.

ELECTROCARDIOGRAPHIC STUDIES ON CHILDREN UNDER TREATMENT BY PNEUMOTHORAX. L. LEONCINI and G. L. PADOVANI, Pediatria **59**:329 (May) 1951.

Electrocardiograms were made on 20 children with tuberculosis, who had been treated by artificial pneumothorax. No myocardial changes were detected which might be traced to this treatment. Right pneumothorax caused a shift of the cardiac axis to the left, but left or bilateral pneumothorax caused practically no change. HIGGINS, Boston.

PERTUSSIS AND STREPTOMYCIN: A CLINICAL, ROENTGENOLOGIC, ALLERGOMETRIC, AND HEMATOLOGIC STUDY. R. BULGARELLI, Policlinico inf. **16**:341 (Aug.) 1948.

An epidemic of whooping cough occurred in a ward of tuberculous children, who were being treated intensively with streptomycin. It appears therefore that streptomycin was not a prophylactic against whooping cough. However, streptomycin had some curative clinical action against whooping cough in that it reduced the number and severity of coughing paroxysms. With streptomycin therapy, whooping cough did not alter the positive reactions of the patients to tuberculin. The tuberculous process in the children treated with streptomycin was not made worse by whooping cough. The blood and bone-marrow changes in the streptomycin-treated children were less marked than those usually found in pertussis. The author believes that streptomycin therapy is justified in whooping cough, but his experience has not yielded the spectacular results claimed by the Belgian physician, Lust. HIGGINS, Boston.

SULFONAMIDES IN TREATMENT OF TUBERCULOSIS: CHEMOTHERAPY, PHARMACOLOGY, TOXICOLOGY. P. PERITI, Riv. clin. pediat. **47**:685 (Oct.) 1949.

The author makes a synthetic reexamination of the antituberculous chemotherapeutic action in men and animals of the different sulfonamide drugs used in the treatment of this disease. Pharmacological and toxicological considerations regarding practical therapy are also discussed.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL SYPHILIS OF THE BONES AND PENICILLIN. JULIO HASBUN and JORGE ROSSELOT, Rev. chilena pediat. **20**:53 (Feb.) 1949.

A detailed study of the roentgenologic findings in 50 infants with congenital syphilis, who were hospitalized and treated with penicillin, is reported. As in the evaluation of any treatment, the possibility of a spontaneous remission must be considered; this possibility is carefully analyzed as regards skeletal changes observed roentgenographically. A standard that will permit subsequent comparison of the regression in the bone lesions following treatment is established.

Roentgenologic study carried out before treatment serves as an approximate standard of spontaneous healing, as it evidences at different ages different degrees and types of bone lesions. McLean's classification as modified by A. Hill is used, since it allows an arbitrary but nevertheless a valuable arithmetic representation of the degree of bone involvement. The essentially dynamic character of congenital bone syphilis is evidenced when one sees the different speeds in the progression of the lesions.

FROM THE AUTHORS' SUMMARY.

ENDONASAL LUPUS TREATED BY CHARPY'S METHOD. ROBERTO INFANTE YAVAR, Rev. chilena pediat. **20**:72 (Feb.) 1949.

The author describes the case of a patient with endonasal lupus treated by administration of vitamin D in large amounts (Charpy's method).

FROM THE AUTHOR'S SUMMARY.

RECURRENCE OF TUBERCULOSIS TREATED WITH STREPTOMYCIN. JAVIER MILLAN V., Rev. chilena pediat. **20**:77 (Feb.) 1949.

The case is reported and analyzed of an 11-year-old girl, in whom, following an appendectomy, miliary, intestinal, and renal tuberculosis developed. She was treated with streptomycin and showed considerable improvement, both clinically and roentgenologically. There remained only a small infiltration of the right lung. Seven months after the surgical intervention, a new miliary distribution associated with a tuberculous meningitis was diagnosed, and shortly afterward, the patient died. This time, streptomycin had not been available.

The effects of surgical intervention and of a general anesthesia upon the evolution of the tuberculous process are analyzed. The brilliant results observed during the first streptomycin treatment are noted.

FROM THE AUTHOR'S SUMMARY.

BULLOUS EMPHYSEMA IN PRIMARY INFECTION OF TUBERCULOSIS IN THE INFANT. JORGE PENA CERECEDA and ALEJANDRO MACCIONI, Rev. chilena pediat. **21**:241 (June) 1950.

The authors present case histories of 11 children with a primary pulmonary complex and simultaneous bullous emphysema.

First the literature is briefly reviewed, then the pathogenesis of this syndrome is summarized, and reference is made to the difficulties in making the differential diagnosis between cavitary caseous pneumonia and atelectasis with bullous emphysema. The authors believe that the roentgenologic findings characteristic of the latter condition, such as the clear outline of the air shadow and the sudden changes of shape and size, are not observed regularly in the primary stage of tuberculous infection, which generally gives irregular and hazy shadows.

From a clinical point of view, in the majority of the cases the symptoms began acutely with signs of great activity and, in some cases, with a marked involvement of this general condition. Nevertheless in all patients the course was eventually favorable whether or not streptomycin was used.

The following concomitant pulmonary lesions were present: adenopathy in 7 cases, pulmonary atelectasis in 10 cases, hematogenous lesions in 2 cases, and endobronchial lesions in 5 of 8 cases in which bronchoscopy was done. These endobronchial lesions were as follows: localized bronchial stenosis in three cases, bronchial perforation in one, and proliferative specific laryngeal lesions in one.

FROM THE AUTHORS' SUMMARY.

HEMIPLEGIC SYNDROME IN TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN. JORGE E. HOWARD, RODOLFO MERELLO, MARIANO LATORRE, and ROBERTO GALECIO, Rev. chilena pediat. **21**:433 (Oct.) 1950.

The authors studied nine children with hemiplegia during the course of a tuberculous meningitis treated with streptomycin. They found that the hemiplegia is always complete and may appear during any stage of the disease. They believe that the productive mechanism is generally a perivascular exudate which obstructs the artery. In order to localize the anatomical process, electroencephalograms and arteriograms were done. One of the arteriograms evidenced obstruction of one of the main arteries. In two cases, postmortem cerebral arteriograms were done, but no evidence of arterial obstruction was apparent.

FROM THE AUTHORS' SUMMARY.

PRIMARY EXTRAPULMONARY TUBERCULOUS COMPLEX IN THE CHILD. JORGE PENA CERECEDA and ENRIQUETA BARILARI, Rev. chilena pediat. **21**:495 (Nov.) 1950.

The authors have studied 41 cases of extrapulmonary tuberculous primary complexes from the clinical, bacteriological, histological, and therapeutic viewpoints. In 23 cases the infection was mucocutaneous, in 14 intraoral, especially tonsillar, and in 4 intestinal. The patients were between 6 months and 14 years old, the majority between 6 and 10 years old. The most frequent localizations were the skin of the lower extremities, the tonsils, the eyes, the intestines, and the genitalia. In most cases the primary lesions were identified because of the characteristic appearance of the accompanying adenopathy, since they did not present typical macroscopic findings which premitted diagnosis.

In the cases of primary tuberculosis of the tonsils the reaction was variable; in some cases there was a marked inflammatory reaction, with or without ulceration, while in others these lesions could be overlooked because of the slight symptomatology, the diagnosis being made by the tuberculous appearance of the submaxillary adenitis.

The source of the tuberculous infection was found in only 14 children. All children had positive reactions to Mendel's test (Mantoux; 1:1,000). In all children the chest roentgenograms were normal in periods ranging from six months to five years. Bacteriological and histological examination of the primary lesions did not elicit positive results in all cases. The authors found tuberculous tissue only in 7 of the 15 children for whom biopsies were done. They offer no explanation for this fact. In some cases the positive findings in the biopsy specimens were established on the 30th day, while in others findings were positive after 14 months. The authors conclude that histological study of the primary lesions has no practical value.

The most important clinical sign in establishing the diagnosis of an extrapulmonary primary complex is the accompanying adenitis. The authors remark on the great involvement of the regional lymph nodes with, in a great number of cases, softening and fistulization. While the results of bacteriological examination were positive in only 6 out of 13 cases, biopsy findings proved positive in all the 19 cases in which biopsy was done. The authors therefore recommend this last procedure.

In 12 cases treatment consisted of local use of streptomycin, with favorable results in 6. In four of these streptomycin had to be used systemically, due to failure of the local treatment or to the appearance of new lymph nodes; results were excellent. In one case local treatment failed, and in another there was improvement even though treatment was insufficient. Eight patients were treated with streptomycin intramuscularly, with favorable results in all in less than two months. Some of these patients are still being treated. In seven patients a mixed treatment was done, with good results in five and a failure in two. In four patients the diseased

lymph nodes were removed, with good results after one to nine months. In seven patients no treatment was done. Six of these were not controlled afterwards and one made a favorable recovery after four months. Only in two of the streptomycin-treated patients was the removal of the adenitis necessary because of caseation.

The authors conclude that streptomycin administered intramuscularly is the treatment of choice for patients with extrapulmonary tuberculous primary lesions. They recommend local treatment by infiltrations of streptomycin in cases of recent adenitis and surgical removal or curettage when the lymph nodes have become caseated or fistulized.

FROM THE AUTHORS' SUMMARY.

PULMONARY TUBERCULOSIS IN THE INFANT. N. MOLL, J. MILLAN, R. MATTE, A. TRAUTMAN and A. VARGAS, Rev. chilena pediat. **22**:200 (May) 1951.

The authors studied 254 necropsies done at Luis Calvo Mackenna Children's Hospital in order to investigate tuberculous lesions. They draw conclusions about primary and postprimary tuberculosis. Reinfection or adult tuberculosis is responsible for not more than 0.9% of all the deaths. Tuberculous meningitis and diffuse miliary tuberculosis are the more frequent types. The primary focus is seen more often in the right lung than in the left, in the same proportion as has been found by other authors.

GRULEE, Evanston, Ill.

MULTIPLE CYSTIC TUBERCULOSIS OF THE BONES COMPLICATED BY TUBERCULOUS MENINGITIS. LUIS VERA CAVIEDES and ROMILDA BANFI B., Rev. chilena pediat. **22**:211 (May) 1951.

The authors report the case of an infant, with typical bone lesions of multiple cystic tuberculous osteitis, with a positive reaction to Mendel's test, with both hilar and paratracheal adenopathies, in whom, during the course of the disease and during streptomycin treatment, meningitis developed, probably from the same origin. Streptomycin was administered exclusively by the intramuscular route, in two doses 12 hours apart. The total dose was 104 gm. in 130 days. Complete healing of the bone lesions was obtained, as well as disappearance of the meningeal symptomatology, and the cerebrospinal fluid remained normal for one year after treatment. The intrathoracic adenopathies regressed to calcification.

GRULEE, Evanston, Ill.

TWO CASES OF PULMONARY TUBERCULOSIS TREATED WITH STREPTOMYCIN. RIGOBERTO AGUILAR and RUBÉN LAVALLE ARGUDÍM, Bol. méd. Hosp. inf., México **5**:825 (Dec.) 1948.

The authors present the cases of two patients with primary pulmonary tuberculosis treated with streptomycin. In the first case there was an exudative pneumonic process and granulitis of the nodular type, and there seemed to be atelectasis of the middle lobe of the right lung. In the second case, also, there was an exudative pneumonic process and granulitis of the miliary type. The atelectasis in this case was confirmed, and it was localized to the upper lobe of the right lung.

The total dose of streptomycin used in the first case was 65.8 gm. over a period of 64 days, and in the second case, 33.6 gm. in 45 days. In both instances, the pulmonary processes had a favorable regression, but the use of the drug did not prevent the development of bronchiectasis.

FROM THE AUTHORS' SUMMARY.

A CASE OF TOXOPLASMOSIS. FELICIANO PALOMINO DENA, RAFAEL SOTO, and LUCINA VILLEGAS LEON, Bol. méd. Hosp. inf., México **7**:24 (Feb.) 1950.

The authors describe what may perhaps be the first case reported of toxoplasmosis in Mexico. The patient was an 11-month-old girl who was first seen on Dec. 21, 1946. At that time only contractures and the presence of intracranial calcifications were found; toxoplasmosis was then suspected, but the diagnosis was not established because of the absence of other positive evidence and especially because of lack of confirmation from laboratory data.

In June, 1947, the patient was seen again; some tests were performed, but no test was made for Toxoplasma because of the lack of antigen. In April, 1949, the patient was hospitalized in

Galveston, Texas. Intracranial calcifications were reported from the roentgenologic studies, and the serologic reaction to a test for toxoplasmosis was positive. Special lesions were found in both fundi.

In the present case, the disease may be considered as of the acquired type, since there was no evidence of modifications in the patient during intrauterine life. The authors expect that, with the presentation of this case, other reports will follow. They offer a few suggestions for making the correct diagnosis of toxoplasmosis and for the prophylactic treatment of pregnant women. Also, they request the preparation of the antigen in our hospitals.

FROM THE AUTHORS' SUMMARY.

PROGNOSTIC EVALUATION OF TUBERCULOUS INFECTION. H. KLEINSCHMIDT, Deutsche med. Wchnschr. **75**:1281 (Sept. 29) 1950.

It is evident that the great mass of tuberculin-positive children without any demonstrable lesions have a good prognosis, although manifestations can occur. Such events happen preponderantly, although not exclusively, in the first year following infection in young children, who demand special care during this time.

AMBERG, Rochester, Minn.

CLINICAL ANALYSIS AND TREATMENT OF BONE-JOINT TUBERCULOSIS. OTTO WIESE, Deutsche med. Wchnschr. **76**:853 (June 29) 1951.

A general survey of bone tuberculosis has been made, with emphasis on treatment.

AMBERG, Rochester, Minn.

DIAGNOSTIC USEFULNESS OF INTRACUTANEOUS TEST REACTION IN ACTINOMYCOSIS. HANS-JURGEN and SIEGFRIED HEINRICH, Deutsche med. Wchnschr. **76**:977 (Aug. 3) 1951.

Intracutaneous tests with vaccine of an Actinomyces israeli strain were carried out for 12 patients with proved visceral actinomycosis. By itself, this test has a rather limited diagnostic value.

AMBERG, Rochester, Minn.

CONTEBEN INJURY: TWO FATAL CASES IN CHILDREN. HARALD THOM, Deutsche med. Wchnschr. **76**:1014 (Aug. 17) 1951.

Two infants, one 10 months old and one 15 months old, were treated with amithiozone ("conteben," "thiosemicarbazone"). The first received 3.325 gm. in 127 days, and the second received 0.306 gm. in 20 days. The tuberculous lesions regressed markedly; then the patients became worse and died. At postmortem examination the main lesion was found to be a totally fatty liver.

AMBERG, Rochester, Minn.

IS BCG VACCINATION OF VALUE? FRITZ KÜSTER, Med. Klin. **44**:849 (July 8) 1949.

On the basis of various reports in the literature the conclusion is reached that vaccination with BCG is of definite value.

AMBERG, Rochester, Minn.

CONTRIBUTION TO THE CLINICAL STUDY AND THERAPY OF CONGENITAL SYPHILIS, WITH SPECIAL CONSIDERATION OF INJURIES DUE TO SPIROCID (STOVARSOL). FELIX SARRAZIN, Med. Klin. **44**:1372 (Oct. 28) 1949.

Of 62 babies with congenital syphilis born at term, 18% died. The death of five of these was directly due to syphilis. Of 11 premature infants, 64% died, and in 2 of these syphilis was the cause of death. Acetarsone (stovarsol®) was administered to 38 patients who were under continuous control. Of these, 35 (92.1%) were cured; in 3 the serologic reactions remained positive. In one case a severe gastrointestinal condition occurred as a result of the medication, in two cases multiform erythema occurred, and in six cases dermatitis was manifested.

AMBERG, Rochester, Minn.

ETIOLOGY AND SPECIFIC DIAGNOSIS OF ACTINOMYCOSIS. F. A. LENTZE, Med. Klin. **45**:992 (Aug. 11) 1950.

Actinomycosis in man arises, with few exceptions, from infection with Actinomyces israeli, a common inhabitant of the healthy mouth and its vicinity. It is a mixed infection of the anaerobic flora of the mouth. Agglutination or complement-fixation tests for diagnosis are unreliable. Subcutaneous injection of an Actinomyces vaccine produces typical focal reaction which is of diagnostic value.

AMBERG, Rochester, Minn.

IS THERE A POSSIBILITY OF A BENEFICIAL INFLUENCE ON PULMONIC TUBERCULOSIS OF CHILDREN BY CONTEBEN? W. HEESEN and A. HEIDWEILER, Med. Klin. **45**:1457 (Nov. 17) 1950.

Amithiozone ("conteben") was administered to 110 children and adolescents, aged 2 to 18 years. Twenty-four patients were 3 to 9 years old, twenty-eight patients were 10 to 14 years old, and fifty-eight patients 15 to 18 years old. For children under 4 years old the dose was 0.025 gm. initially and then increased to 0.05 gm., and occasionally to 0.075 gm. Even so, fatigue, vomiting, headache, and increased thirst were noted. The medication was given for a year. Definite proof of beneficial activity of the drug on the tuberculosis of the lung in these patients could not be demonstrated.

AMBERG, Rochester, Minn.

SODIUM AND POTASSIUM LEVELS OF THE CEREBROSPINAL FLUID IN TUBERCULOUS MENINGITIS. URBAN, Monatsschr. Kinderh. **98**:145 (April) 1950.

Values for Na and K in the cerebrospinal fluid were normal in patients with tuberculous meningitis. Low Na levels were found with high K levels and vice versa, all, however, within normal limits. In the early stages of the disease relatively high Na levels and low K levels were noted; later Na decreased and K rose. Persistent relatively high K values and low K values were found in patients with chronic tuberculous meningitis running a favorable course.

HARTENSTEIN, Madison, Wis.

TOXOPLASMOSIS IN CHILDREN. HELMUT WALENZ and ALBERT WESTPHAL, Monatsschr. Kinderh. **98**:329 (Aug.) 1950.

Four cases of congenital toxoplasmosis are reported. Three of them showed hydrocephalus, neurological manifestations, chorioretinitis, and changes in the cerebrospinal fluid. In the other patient only chorioretinitis and minimal cerebrospinal fluid changes were noted. Intracerebral calcification, upon roentgenologic examination, were not seen in any of the patients. The reaction to a serum dye test (Sabin and Feldman) was positive in all cases. Intrauterine transmission of the disease was proved by demonstrating positive titers in the blood of all the mothers. In two of the infants parasites were demonstrated in the cerebrospinal fluid or by animal passage.

HARTENSTEIN, Madison, Wis.

TREATMENT OF CONGENITAL SYPHILIS WITH A COMBINATION OF PENICILLIN AND SPIROCID. K. STENGER, Monatsschr. Kinderh. **98**:369 (Sept.) 1950.

Forty-eight infants and children with congenital syphilis were treated in the following manner. Crystalline penicillin was administered intramuscularly in a dosage of 10,000 units per kilogram of body weight every 10 days (eight injections per 24 hours). An eight-day rest period followed. Then the above penicillin regimen was repeated, and another eight-day rest period followed. The schedule of acetarsone ("spirocid") treatments was as follows: ½ to 1 tablet daily for 10 days, a rest for four days, then 1 to 2 tablets daily for 10 days. (Each tablet of acetarson contained 0.25 gm.)

Four patients died, death being due not to the treatment but to the severity of the disease, as demonstrated at autopsy. Serologic reactions became negative in all patients treated. All surviving patients improved rapidly during therapy. Febrile reactions after initiation of penicillin therapy occurred in about 50% of all cases.

HARTENSTEIN, Madison, Wis.

PATHOLOGIC-ANATOMICAL OBSERVATIONS IN PATIENTS WITH TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN. H. CHIARI, Wien. klin. Wchnschr. **60**:837 (Dec. 31) 1948.

The author discusses the results of histologic examination of 10 patients with tuberculous meningitis, after treatment with streptomycin for 4 to 92 days, with a duration of the disease from 8 to 255 days. With the exception of a 16-year-old boy, the patients were 5 months to 6¾ years old. The findings are summarized to show that in the leptomeninges productive processes are prominent, with the formation of connective tissue rich in fibers but still containing tubercles.

AMBERG, Rochester, Minn.

HEMATOGENOUS TUBERCULOSIS AND MANGANESE CHLORIDE. V. GORLITZER, MUNDY, Wien. klin. Wchnschr. **61**:539 (Aug. 26) 1949.

About 100 years ago Kugler reported that workers in a manganese factory remained surprisingly free of scrofulosis. Later, manganese chloride was found by Walbum to be particularly efficient in the treatment of experimental hematogenous tuberculosis. Two cases are reported in which tuberculous meningitis yielded to rectal administration of 1 ml. of 0.02 molar solution of manganese chloride, given once or twice daily for about 10 days.

AMBERG, Rochester, Minn.

TUBERCULOUS MENINGITIS AND STREPTOMYCIN. E. MICHIELS, Acta pædiat. belg. **4**:211, 1950.

Ninety children, in two groups (one those below and one those above 6 years of age), were treated uniformly with daily intrathecal injections of 50 and 100 mg., respectively, of streptomycin for a period of six weeks, and with daily intramuscular injections of 50 mg. per kilogram of body weight for six months. Following this period of therapy, the patients received two-day therapy for 3 to 4 months, three times per month.

The greatest number of deaths occurred during the first month of treatment. The death rate was highest in those who began treatment late, in the very young (below 2 years of age) and in those who had pulmonary involvement. Thirty-eight per cent of the patients survived with excellent results. Relapses occurred in 43% of the patients who survived six weeks of treatment, and they occurred as early as the 3d month of treatment and as late as the 17th. Pulmonary involvement and the discontinuation of intramuscular therapy seemed to increase the number of relapses.

The author concludes that prolongation of intramuscular therapy and more intensive therapy in cases of pulmonary involvement may reduce relapses. The value of the prolongation of intrathecal therapy is under study in a second series of patients who were given a second course of six weeks of intrathecal injections every second day.

GLASER, Jerusalem, Israel.

X-RAY EXAMINATION OF THE VENTRICULAR SYSTEM OF CHILDREN SUFFERING FROM TUBERCULOUS MENINGITIS. I. FLESCH and C. GEFFERTH, Pediat. danub. **5**:158 (March-April) 1949.

A method has been devised for visualizing the ventricles of patients suffering from tuberculous meningitis treated with streptomycin. The procedure proved to be less dangerous than pneumoencephalography and is, therefore, more suitable for serial examinations. Five to fifteen milliliters of air are insufflated into the spinal canal after lumbar puncture, and the skull is examined in different positions from various directions behind the roentgenographic screen. Exploratory examinations were carried out 195 times on 72 patients suffering from meningitis. The method, which has no danger, yields only superficial information but is still of great value for diagnostic purposes and for evaluating therapeutic measures.

It could be ascertained by the aid of the method that hydrocephalus is an early and very frequent sequela. Obstructions and destructive processes could well be demonstrated. In two cases porencephaly was noted.

FROM THE AUTHORS' SUMMARY.

STATISTICS ON TUBERCULIN TEST RESULTS ON SCHOOL CHILDREN IN PRAGUE. A. ZAHALKOVA, Pediat. listy **5**:290, 1950.

The methods, results, and significance of the statistics on tuberculin-test positivity of school children in Prague are described. The number of children tested was 64,535 in the years 1947-1948, and 75,560 in 1948-1949. The results are shown in the following tabulation and compared with results from the year 1925.

| Elementary School, Class | Percentage of Tuberculin-Positive Children | | |
|---|---|---|---|
| | 1925 | 1947-1948 | 1948-1949 |
| I | 40.04 | 14.6 | 13.7 |
| II | 45.78 | 20.2 | 20.3 |
| III | 50.78 | 23.4 | 25.4 |
| IV | 56.12 | 24.6 | 28.8 |
| V | 60.67 | 30.6 | 30.4 |
| **Middle School, Class** | | | |
| I | 60.47 | 36.2 | 33.7 |
| II | 63.07 | 37.6 | 35.1 |
| III | 63.13 | 39.0 | 34.7 |
| IV | ..... | 37.7 | 41.7 |

This study shows clearly that the percentage of children with positive reactions decreased considerably and that the time when infection takes place changed to the upper age groups. Further comparative studies will not be possible because practically all school children of Prague have now been vaccinated with BCG vaccine.

FROM THE AUTHOR'S SUMMARY.

PRIMARY TUBERCULOSIS AT THE SITE OF THERAPEUTIC INJECTIONS. J. HOUSTEK and G. VOLNA, Pediat. listy **6**:336, 1950.

Primary tuberculosis of the skin at the site of therapeutic injections is reported in three boys and two girls. In four cases the disease very probably followed pencillin injections, and in one case it followed injection of ascorbic acid. The primary lesion was threefold in one child; in the others it was in one extremity. One of the children died eight months after the onset of the disease and five months after streptomycin treatment had been started. The remaining four children are in excellent general health.

FROM THE AUTHORS' SUMMARY.

MENINGITIS DUE TO BACILLUS TYPHOSUS. S. CHAROCOPOS and N. MOSCHOS, Acta Soc. pediat. hellen. **3**:242 (Nov.-Dec.) 1949.

A 6-year-old girl was febrile for 39 days, with a severe attack of typhoid. Return to normal temperature was followed by general improvement, but 11 days later the temperature rose again, and signs of meningitis appeared. The cerebrospinal fluid was purulent, and the Salmonella typhosa (Bacillus typhosus) was cultured from it. The patient died 15 days after the onset of meningitis, in spite of treatment with pencillin and streptomycin. Chloramphenicol was not available. Meningitis due to S. typhosa is a rarity, since none was encountered among 1,685 cases of typhoid in children, previously reviewed by one of the authors (S.C.).

DOXIADIS, Sheffield, England.

STUDIES OF A TOXOPLASMOTIC FAMILY: SULFATHIAZOLE PROPHYLAXIS. GUNNAR ENGLESON, Acta pædiat. **37**:359, 1949.

A woman who had previously given birth to a child with toxoplasmosis was again pregnant. Sulfathiazole prophylaxis was used, and toxoplasmosis did not develop in this child.

FROM THE AUTHOR'S SUMMARY

STREPTOMYCIN IN MILIARY TUBERCULOSIS AND TUBERCULOUS MENINGITIS. A. LICHTENSTEIN, Acta pædiat., supp. 75, p. 5, 1949.

Hematogenic tuberculosis can be cured by streptomycin. The author stresses the fact that up to now only about 10 to 15% of patients have been cured. He points out that a number of factors concerning streptomycin are still obscure, that streptomycin is toxic, and that its effect is mainly bacteriostatic.

FROM THE AUTHOR'S SUMMARY.

THE ELECTROENCEPHALOGRAM IN CASES OF TUBERCULOUS MENINGITIS. A. LICHTENSTEIN AND K. A. MELIN, Acta pædiat., supp. 75, p. 75, 1949.

Electroencephalographic examination of seven children with streptomycin-treated tuberculous meningitis showed that clinical deterioration, which occurred in three cases, was accompanied by electroencephalographic changes in the form of large (4 to 5 per second) waves. In one case electroencephalographic changes were the first indication of deterioration. In four patients, who were restored to complete or almost complete health, the changes noted earlier in the disease disappeared. Thus, repeated electroencephalographic recordings may be of prognostic value and may even indicate a need for intensified treatment.

FROM THE AUTHORS' SUMMARY.

DIAGNOSTIC DIFFICULTIES AND POSSIBILITIES IN TUBERCULOUS MENINGITIS. W. VAN ZEBEN, Maandschr. kindergeneesk. **18**:45, 1950.

Since isolation of tubercle bacteria from cerebrospinal fluid takes a long time and since we do not always succeed in finding bacteria by direct microscopic examination, diagnosis is made at first on the basis of clinical and pathological data. Difficulties can arise when infection with tuberculosis is unknown and when the typical changes of the cerebrospinal fluid are absent. In these cases the clinical course and changes of the cerebrospinal fluid must be followed closely. Institution of streptomycin therapy must be delayed until a correct diagnosis has been made. In one case a lymphocytic meningitis was accompanied by a focus in one lung. The course of the disease and the presence of cold agglutinins made virus infection probable. In one patient it was possible to demonstrate an internal hydrocephalus; thus it was possible to make the diagnosis of tuberculous meningitis before typical changes of the cerebrospinal fluid had developed. In patients suffering from miliary tuberculosis, however, intrathecal administration of streptomycin should be instituted as soon as slight changes in the cerebrospinal fluid are found.

VAN CREVELD, Amsterdam, Netherlands.

RELATION BETWEEN PATHOGENESIS OF TUBERCULOUS INFECTION AND COURSE OF TUBERCULOUS MENINGITIS IN CHILDREN TREATED WITH STREPTOMYCIN. A. DE MINJER, Maandschr. kindergeneesk. **18**:285, 1950.

On 11 children with tuberculous meningitis, who had been treated with streptomycin and died, postmortem examination was done. On the basis of the course of the disease the cases could be divided into two groups. In the five children of the first group streptomycin treatment had not had any influence upon the course of the disease. In the other six children life had been prolonged by streptomycin therapy, and some of the patients had shown clinical improvement. At autopsy the first five patients had an extensive recent primary complex and a widespread dissemination in many organs. All patients in the second group had a small primary complex, which was already calcified. The foci of hematogenous dissemination had also nearly healed in these cases.

Therefore, in the first group tuberculous meningitis as well as hematogenous dissemination followed the primary infection closely. In that period the immunity of the children must still have been weak, which may account for the rapid progression of the inflammation of the meninges. The children of the second group, however, had conquered the primary infection and gained some degree of immunity. Minjer considers the hematogenous dissemination and inflammation of the meninges in the second group as an incidental occurrence. The rapid dissemination in the first group is explained by mass infection. This is supported by the presence of multiple primary foci in the patients of the first group. Four out of five children had had close contact with patients suffering from tuberculosis.

VAN CREVELD, Amsterdam, Netherlands.

FREQUENCY AND DURATION OF EXPECTORATION OF TUBERCLE BACILLI IN THE PRIMARY AND SUBPRIMARY FORMS OF LUNG TUBERCULOSIS. C. DIJKSTRA, Maandschr. kindergeneesk. **19**:119 (June) 1951.

The results of frequent sputum culture tests in 106 patients suffering from primary and postprimary forms of pulmonary tuberculosis are discussed, with reference to three graphs. In 82% of the patients with still-active lung lesions, excretion of tubercle bacilli continued for periods varying from 1 to 20 months. Eighteen patients underwent active treatment, 5 of them by collapse therapy and 13 by lobectomy. Two patients died of progressive pulmonary disease. Nine patients (8.5% of the total number), after the lung process had become clinically inactive, still had intermittent excretion of tubercle bacilli. Sixteen patients (15% of the total) showed no further excretion of tubercle bacilli for at least five months before the end of the sanatorium treatment (when 10 successive sputum cultures or cultures of the gastric lavage were negative). Owing to the fact, however, that prolonged intermissions in the excretion of tubercle bacilli had previously occurred, it is doubtful if the pulmonary processes may be considered as really "closed" in these cases.

In 79 cases (that is 74.5% of the total) the sputum became apparently permanently free of bacilli, although at the beginning of the disease a more or less regular discharge of tubercle bacilli had existed for variable lengths of time.

FROM THE AUTHOR'S SUMMARY.

BCG VACCINATION: ELEVEN YEARS OF EXPERIENCE. Y. CH. LIEOU and C. C. KOUO, Chinese M. J. **667**:275 (May) 1949.

The Shanghai Pasteur Institute has used the following three methods of BCG vaccination. 1. BCG vaccine was administered orally to 7,511 children. Starting 10 days after birth, 10 mg. was administered every other day for three doses. No harmful effects were seen. No tuberculin tests were done. 2. Four hundred forty-four tuberculin-negative children received BCG vaccine intracutaneously. The usual dosage was 100 mg. in four doses. Of these children, 90% became tuberculin-positive. An abscess developed at the site of vaccination in 8%. 3. In 645 children vaccination was done by scarification according to the method of Negre and Bretey. Of these children 97.4% became tuberculin-positive after vaccination. No complications were encountered. In 11 years no active tuberculosis in these vaccinated children has been reported to the Institute.

MACDONALD, Pittsburgh.

## Diseases of Blood, Heart and Blood Vessels and Spleen

A CASE OF LETTERER-SIWE DISEASE. CHARLES WADSWORTH SCHWARTZ, Am. J. Roentgenol. **65**:931 (June) 1951.

Letterer-Siwe disease is characterized by hepatic and splenic enlargement, purpura, secondary anemia, lymphadenopathy, and a rapid downhill course. The disease is included among the reticuloses and is thought by some to be an acute form of Schüller-Christian disease. Others have felt that it may be an early form of Schüller-Christian disease. The roentgenograms in the case presented showed extensive involvement by the osteolytic lesions of reticuloendotheliosis, and an autopsy report is included in the paper.

HODGSON, Rochester, Minn.

CONGENITAL GLYCOGENIC TUMORS OF THE HEART. LEWIS A. KIDDER, Arch. Path. **49**:58 (Jan.) 1950.

A case of multiple congenital glycogenic tumors of the heart of a newborn infant is reported, constituting the 69th case on record in the literature. Glycogen was demonstrated, and cross striations were seen within the cells. An area of giant astrocytes compatible with, but not pathognomonic of, tuberous sclerosis was observed in the brain. The literature is reviewed, and it is noted that tuberous sclerosis is the most frequently associated lesion, with renal lesions (tumors, cysts, and anomalies) the second most frequent. The author believes that the cause of glycogenic tumors of the heart is probably related to a glycogen-storage disturbance.

CHAN, San Francisco.

THE DISTRIBUTION OF FREE AMINO ACIDS BETWEEN ERYTHROCYTES AND PLASMA IN MAN. CLARENCE A. JOHNSON and OLAF BERGEIM, J. Biol. Chem. **188**:833 (Feb.) 1951.

Plasma and red cell levels of 12 free amino acids were determined on single blood specimens obtained from 24 normal young men in a postabsorptive state. The plasma was found to contain four to six times as much cystine, tryptophan, and arginine as the red cells and somewhat more histidine, valine, lysine, and isoleucine. Values for phenylalanine, tyrosine, methionine, threonine, and leucine were roughly the same in plasma and in red cells.

FORBES, Dallas, Texas.

THE HEMOGLOBIN CONCENTRATIONS, ERYTHROCYTE COUNTS, AND HEMATOCRITS OF SELECTED LOUISIANA ELEMENTARY SCHOOL CHILDREN. MARA McBEE, DOROTHY S. MOSCHETTE, and CLARA TUCKER, J. Nutrition **42**:539 (Dec. 11) 1950.

For 515 Louisiana school children studied, 86.9% of the hemoglobin values, 91.9% of the erythrocyte counts, and 96.3% of the hematocrit values were within the generally accepted normal range for children from 8 to 13 years old. The corpuscular values were compared with the ranges of these values given by Sturgis (1948) and also by Wintrobe (1946) in classifying anemias. Seventy-five per cent of the Louisiana children were normal according to these standards.

FREDEEN, Kansas City, Mo.

AORTIC ATRESIA WITH HYPOPLASIA OF THE LEFT HEART AND AORTIC ARCH. SIDNEY FRIEDMAN, LOIS MURPHY, and RACHEL ASH, J. Pediat. **38**:354 (March) 1951.

The cases of four male infants with congenital heart disease are reported. None lived longer than 18 days. The combination of anomalies included (1) atresia or stenosis of the aortic valve; (2) hypoplasia of the left atrium, mitral valve, left ventricle, and aortic arch; (3) hypertrophy and dilatation of the right atrium, right ventricle, and pulmonary artery; (4) a functioning patent ductus arteriosus, and (5) a patent foramen ovale or some other anomalous pathway for the transport of blood from the left to the right atrium.

Cyanosis and dyspnea were seen in all patients. Precordial murmurs were not always present but, when heard, were systolic in time and best heard to the left of the sternum. Roentgenograms showed massive cardiac enlargement. Because of the profound distortion of hemodynamics, there is little reason to believe that cardiac surgery might have helped these patients.

MACDONALD, Pittsburgh.

HEMANGIOMA ASSOCIATED WITH THROMBOCYTOPENIC PURPURA. SAMUEL C. SOUTHARD, ADOLPH G. DESANCTIS, and ROBERT J. WALDRON, J. Pediat. **38**:732 (June) 1951.

The patient reported upon here was a 21-day-old infant with a large hemangioma of the left thigh and an associated thrombocytopenic purpura. The authors observed that the megakaryocytes were not abnormal when the platelet count was low. When the child was treated with blood transfusion and x-rays, the platelet count rose to normal one week after therapy was started. This is the fourth such case in the literature.

MACDONALD, Pittsburgh.

EVOLUTION OF SYSTEMIC RETICULOENDOTHELIOSIS IN CHILDHOOD. PAUL FREUD, J. Pediat. **38**:744 (June) 1951.

The author defines systemic reticuloendotheliosis as the proliferative response of the embryonal reticulum cells of the body to a stimulating agent. He has reviewed the literature on acute reticuloendotheliosis (Letterer-Siwe disease), chronic reticuloendotheliosis (Schüller-Christian disease), and eosinophilic granuloma. He says that all of these diseases are different phases of the same basic disorder. Schüller-Christian disease should not be linked to Gaucher's disease and Niemann-Pick disease. These latter two are hereditary familial lipidoses. The cholesterol in the proliferating cells of Schüller-Christian disease is not the result of a fundamental humoral disturbance of lipid metabolism. It is more akin to fatty cellular degeneration. Freud suggests the term cholesterol degeneration.

To the three forms of systemic reticuloendotheliosis mentioned, Freud has added a case report in detail. This case of reticuloendotheliosis was characterized by early xanthomatosis with later leucemic response.

MACDONALD, Pittsburgh.

SICKLE-CELL ANEMIA. FREDERICK J. HELDRICH JR., J. Pediat. **39**:90 (July) 1951.

Heldrich reports a case of sickle-cell anemia in a newborn Negro girl. Jaundice and epistaxis developed during the first few days of life. One sibling has sickle-cell anemia, and both parents show evidence of sicklemia. This is the youngest patient with sickle-cell anemia ever reported upon.

MACDONALD, Pittsburgh.

CAVERNOUS HEMANGIOMA OF THE THORACIC WALL ASSOCIATED WITH CLINICAL EVIDENCE OF ARTERIOVENOUS FISTULAS. TIMOTHY TAKARO and O. THERON CLAZETT, J. Thoracic Surg. **21**:444 (May) 1951.

Cavernous hemangiomas of the thoracic wall have been reported in the literature from time to time. However, such lesions associated with arteriovenous fistula of the intercostal vessels have never been reported. The authors report the case of a 40-year-old white man who had noticed a tumor mass in the left posterior axillary line for 18 months. Upon physical examination a soft pulsating tumor, 6 by 12 cm., was observed. Upon auscultation, a bruit with systolic and diastolic components was heard. A roentgenogram of the chest showed scalloping defects of the seventh, eighth, and ninth ribs in the area of the mass. The lesion was successfully removed surgically.

MEYER, Chicago.

INFANTS UNDER ONE YEAR OF AGE WITH TETRALOGY OF FALLOT OR TRICUSPID ATRESIA. C. R. LEININGER and S. GIBSON, Pediatrics **7**:341 (March) 1951.

Since September, 1946, surgical relief for tetralogy of Fallot or tricuspid atresia has been performed in 234 instances. During this period anastomosis has been created in 24 infants under one year old. Pulmonary atresia prevented an anastomosis in two additional infants. In those children in whom an anastomosis was possible, the mortality was 33.3% under 1 year of age as compared to an over-all mortality of 9.8% and a mortality of only 2.9% between the ages of 3 and 16 years.

The reasons for the higher mortality in infants are explained, and surgical relief in selected cases is recommended.

FROM THE AUTHORS' SUMMARY.

VOLUMETRIC AND MICROSCOPIC PATTERN OF BONE MARROW IN NORMAL INFANTS AND CHILDREN: III. HISTOLOGIC PATTERN. PHILLIP STURGEON, Pediatrics **7**:774 (June) 1951.

In normal infants 3 months old or younger, particles obtained from the bone marrow by the described aspiration technic may be comprised of 80% or more hemopoietic tissue. Particles obtained by aspirations of the sternum and iliac crest from normal children 19 months through 11 years old may vary from 35 to 80% of hemopoietic tissue. Aspirations from the tibia of normal persons 4½ years of age or older may contain 20% or less hemopoietic tissue. No lymph follicles were found in serial sections of particles from 23 normal children 3 days through 11 years old.

FROM THE AUTHOR'S SUMMARY.

COARCTATION OF AORTA AS CAUSE OF DEATH IN EARLY INFANCY. R. C. BAHN, J. E. EDWARDS, and J. W. DUSHANE, Pediatrics **8**:192 (Aug.) 1951.

This is an analysis of the condition of three infants who died of left ventricular cardiac failure as the result of coarctation of the aorta with poorly developed collateral circulation. In each instance the site of coarctation lay opposite a closed or closing ductus arteriosus.

In coarctation of the aorta the position of the coarctation with respect to the location of the entrance of the ductus arteriosus into the aorta will determine whether or not collateral vessels adequate to bypass the coarctation will develop in fetal life. If the coarctation lies beyond the ductus arteriosus, collateral vessels necessarily develop during fetal life if the fetus survives. In cases in which the coarctation lies proximal to the entrance of the ductus arteriosus, the fetal circulation is little, if at all, disturbed, and collateral vessels do not seem to develop during fetal life. In these patients, after the ductus arteriosus closes, the presence of coarctation with inadequately developed collateral vessels causes left ventricular strain and failure. Postnatally collaterals may develop in this type of case if the infant survives. In the group of cases in

which the coarctation lies opposite the ductus arteriosus, adequate collateral vessels develop in the fetus in some cases but in others do not. Whether collateral vessels develop in this type of case seems to depend upon the direction of predominant flow from the ductus into the aorta. When the predominant flow is into the descending aorta, collateral vessels will not develop. In those cases in which the ductus flow is predominantly into the proximal aorta, adequate collateral vessels will develop during fetal life.

The condition of the three patients concerned in this study constituted examples in which there was coarctation of the aorta opposite the ductus and in which inadequate collateral circulation had formed. The effects of this, in the presence of a closed or closing ductus arteriosus, were obstructive hypertension, left ventricular strain, and, ultimately, left ventricular failure. Failure to attempt palpation of the femoral pulses may have been responsible for failure to make the correct clinical diagnosis.

FROM THE AUTHORS' SUMMARY.

ANEURYSMS OF THE SINUSES OF VALSALVA, WITH REPORT OF A CASE. RICHARD E. L. FOWLER and HAROLD H. BEVIL, Pediatrics **8**:340 (Sept.) 1951.

A case of aneurysm of a sinus of Valsalva, with rupture, in a 4-year-old girl is presented. This is believed to be the youngest patient with rupture as yet reported.

Studies of the patients undertaken in an attempt to verify the diagnosis in vivo, included cardiac catheterization, which yielded results compatible with a stream of arterial blood entering the venous circulation at the level of the right ventricle; arterial-oxygen analysis, and oxygen-uptake determination. From figures obtained by these procedures the extent of the left-to-right shunt was calculated to be about 18% of the systemic blood flow. An attempt was made to correlate the unusually benign clinical course with the results obtained from these procedures.

FROM THE AUTHORS' SUMMARY.

SUTURE-LIGATION OF THE PATENT DUCTUS ARTERIOSUS IN INFANCY. W. T. MUSTARD. Canad. M. A. J. **64**:243 (March) 1951.

Four patients with patent ductus arteriosus were operated upon between the ages of 4 and 15 months. Diagnosis was confirmed by aortography. Results were good in all cases and life-saving in patients with cardiac failure. The author concludes that the operation is safe for infants.

McGUIGAN, Evanston, Ill.

STUDIES IN ANAEMIA OF INFANCY AND CHILDHOOD. MARGARET HORAN, Arch. Dis. Childhood **25**:110 (June) 1950.

A report is made of a study of 249 infants in an attempt to establish normal values in the blood picture for infants, to account for the disparity between the findings of different investigators, and to determine whether all infants should receive prophylactic doses of iron compounds in their first year of life. The technique used is described, and the results of approximately 1,200 blood counts are analyzed.

The hemoglobin curve of breast-fed infants in this series was close to that found by other investigators, and after the age of 6 months was practically identical with that found by Mackay, also working with English subjects. In no one age group, however, was there any statistical difference between the hemoglobin values in breast-fed infants, artificially fed infants, or infants fed on a mixture of breast and cow's milk; but, upon averaging the results of all age groups, it was found that the means of the three methods of feeding were significantly different, the highest being in breast-fed infants and the intermediate in infants only partly breast-fed. At 12 months of age the difference between the hemoglobin levels of artificially fed infants and those receiving iron compounds were statistically significant, the iron-treated group having the higher figure. The differences in hemoglobin values recorded by various investigators appear to have a fundamentally racial basis.

KELLY, Milwaukee.

RETICULOENDOTHELIAL GRANULOMA: A REVIEW WITH A REPORT OF A CASE OF LETTERER-SIWE DISEASE. ALBERT E. CLAIREAUX and IAN C. LEWIS, Arch. Dis. Childhood **25**:142 (June) 1950.

The authors present a case of Letterer-Siwe disease, and the clinical and pathological features are described.

The relationship between Letterer-Siwe disease, Schüller-Christian disease, and eosinophilic granuloma of bone is discussed, and the authors suggest that these three conditions are all examples of reticuloendothelial granuloma. Letterer-Siwe disease is the severest and most fatal form, and the prognosis is uniformly bad. Eosinophilic granuloma of bone is the mildest type and frequently occurs as a single lesion. Schüller-Christian disease occupies an intermediate position; the outlook is better than in Letterer-Siwe disease but less favorable than in eosinophilic granuloma of bone.

KELLY, Milwaukee.

LETTERER-SIWE'S SYNDROME: REPORT OF A CASE WITH UNUSUAL PERIPHERAL BLOOD CHANGES. N. P. ORCHARD, Arch. Dis. Childhood **25**:151 (June) 1950.

A case of reticulum-cell medullary reticulosis with peripheral blood changes is described. The white blood cell count fluctuated between a low normal and frank leucopenia, with lymphocytes as the predominant cells; a fair number of hemohistiocytes were invariably present. The reticulum cells showed unmistakable differentiation in two directions, hemic and histiocytic. The hemohistiocytes in the peripheral blood and in the marrow were similar to the proliferating reticulum cells in the lymph glands, spleen, liver, lungs, and kidney. They were medullary reticulum cells with a tendency, as far as the nuclear structure was concerned, toward hemic differentiation. Definite evidence of differentiation towards histiocytes was seen in the liver, spleen, lungs, kidney, and, to a less extent, in the lymph nodes. Apart from a few departures from the accepted picture of Letterer-Siwe disease, namely, the presence of hemohistiocytes in the peripheral blood and the absence of purpura and osseous changes, the case reported satisfies the criteria laid down by Siwe. The Wassermann and Kahn reactions were strongly positive on two occasions, but negative on the third. This no doubt was due to the change in the plasma globulin.

KELLY, Milwaukee.

CHRONIC CARDITIS IN A CHILD OF 19 MONTHS. B. E. MCCONNELL, Arch. Dis. Childhood **25**:186 (June) 1950.

The case is reported of a child, who died at the age of 19 months, in whom necropsy revealed a cardiac lesion suggestive of chronic rheumatic carditis.

KELLEY, Milwaukee.

ERYTHROGENESIS IMPERFECTA. I. A. B. CATHIE, Arch. Dis. Childhood **25**:313 (Dec.) 1950.

Five cases of so-called congenital hypoplastic anemia are reported. The history of one case is described in detail. The condition is characterized by failure of blood regeneration and by reticulocytosis in spite of the presence of some erythroblasts in the marrow. There was a similarity of the facies of the five children.

The results of marrow cultures indicate that red cell maturation fails at the late normoblast stage. The etiology and lack of response to all forms of treatment except blood transfusion are discussed. The term erythrogenesis imperfecta is proposed for the condition, as being less misleading than other descriptive titles.

KELLY, Milwaukee.

TECHNIQUE OF CARDIAC CATHETERIZATION, ITS ROLE IN DIAGNOSIS OF CONGENITAL HEART DISEASE. AMOR SEN, R. CHATTERJEE, and G. MUKHERJEE, J. Indian M. A. **20**:140 (Jan.) 1951.

A brief description of cardiac catheterization is presented. It is too brief to be of value.

MCGUIGAN, Evanston, Ill.

TREATMENT OF BANTI'S SYNDROME IN INFANTS BY SPLENECTOMY AND LIENORENAL ANASTOMOSIS. P. SANTY and P. MARION, Pédiatrie **39**:433, 1950.

The results in the treatment of Banti's disease with splenectomy alone have not been satisfactory. The authors suggest manometric evaluation of the portal pressure by introducing a rubber catheter attached to a manometer into the splenic vein after splenectomy. If the pressure is above normal (normal, 12 cm. of water), anastomosis of the splenic vein with the left renal vein is to be performed. The reason for increased portal pressure may be intrahepatic (cirrhosis) or extrahepatic (congenital, inflammatory thrombosis). Injection of a contrast medium through the splenic vein permits the determination of the cause of portal hypertension and gives more specific indications for surgical procedures. The authors' experience covers eight operations, with no fatalities and a maximal postoperative observation period of 18 months.

GLASER, Jerusalem, Israel.

PERSISTENT DUCTUS ARTERIOSUS AND ITS SURGICAL TREATMENT. C. LIAN and J.-J. WELTI, Presse méd. **58**:389 (April 8) 1950.

Diagnosis of persistent ductus arteriosus rests primarily on the presence of a to-and-fro murmur at the second left interspace. Other causes of such a murmur must be eliminated, e. g., jugular continuous venous hum or arteriovenous aneurysm. Before tying off the ductus, the surgeon must make sure that it is not the safety valve for some other cardiac anomaly.

In 85 patients studied, 16 were operated upon, with favorable results in all.

DAFFINEE, Melrose, Mass.

DORSAL AUSCULTATION OF MURMURS ASSOCIATED WITH CARDIOVASCULAR LESIONS. C. LIAN and DANG-VAN-CHUNG, Presse méd. **58**:585 (May 27) 1950.

Auscultation of the back provides additional evidence of value in diagnosing cardiovascular lesions. The systolic murmur of coarctation of the aorta is louder in back than in front and can be detected over the intercostal arteries. The murmur of an aneurysm of the descending aorta can be heard beside the vertebral column. In cyanotic patients without signs of congenital heart disease, a continuous murmur in back signifies the presence of intrapulmonary arteriovenous aneurysm.

The systolic murmur of mitral insufficiency is transmitted to the left lower posterior thorax. An interventricular communication will often be transmitted to the back, sometimes on the right as well as on the left. Only the systolic phase of the murmur of a persistent ductus arteriosus is transmitted to the back.

DAFFINEE, Melrose, Mass.

SPLENOPATHIC PANHEMOCYTOPENIA. F. HAUSER, Ann. pædiat. **175**:87 (July-Aug.) 1950.

The case is described of a 14-year-old boy with splenopathic panhemocytopenia. He suffered from hemorrhagic diathesis due sometimes to extreme thrombocytopenia, and from severe leucopenia and neutropenia. There was moderately severe anemia. At the same time, the spleen was found to be constantly enlarged, and the bone marrow puncture disclosed many cells. As there was no evidence to indicate that the enlargement and hypertrophy of the spleen were secondary, the condition was assumed to be a primary splenopathy. Splenectomy had an excellent result, and the boy developed, in the two years after operation, into a strong and healthy youth.

The findings in this case make it likely that, besides a decreased activity of the bone marrow, phagocytosis in the spleen must have been excessive. Splenectomy cured the anemia completely, the platelets became normal, the leucocyte count was at the lower level of normal at the last control examination (5,000 to 6,000), while a marked neutropenia persisted. An examination of the patient's parents showed a certain tendency toward neutropenia, but the evidence from the normal was not sufficient to form a conclusion.

FROM THE AUTHOR'S SUMMARY.

CLINICAL PICTURE OF ISTHMUS STENOSIS OF THE AORTA IN THE FIRST MONTHS OF LIFE. S. BUCHS, Ann. pædiat. **175**:102 (July-Aug.) 1950.

The clinical picture of isthmus stenosis of the aorta during the first few months of life differs from that observed in later life. Because of the circulatory failure, the impression of a general disease is created. The primary symptoms and their sequelae are described, and an attempt is made to explain them.

FROM THE AUTHOR'S SUMMARY.

PYRORACEMIC ACID IN CHILDREN UNDER NORMAL AND PATHOLOGICAL CONDITIONS. EMIL PASSWEG, Ann. pædiat. **175**:135 (July-Aug.) 1950.

The content of pyruvic (pyroracemic) acid in the blood was determined in healthy children as well as in children with various illnesses of infancy and childhood. The normal value of pyruvic acid was found to be 0.69 mg. per 100 cc. Pathological values were found in non-controlled diabetes (maximum, 3.2 mg. per 100 cc.), in severe gastroenteritis (maximum, 2.8 mg. per 100 cc.), in acidotic vomiting (maximum, 2.4 mg. per 100 cc.), in toxic influenza cases (maximum, 1.8 mg. per 100 cc.), in hypochloremic states (maximum, 1.6 mg. per 100 cc.), after inanition (1.5 mg. per 100 cc.), in some chronic illness with very bad general health (maximum, 2.0 mg. per 100 cc.), and in a case of sleeping-drug poisoning after prolonged vomiting (2.0 mg. per 100 cc.).

FROM THE AUTHOR'S SUMMARY.

A CASE OF CONGENITAL FAMILIAL AFIBRINOGENEMIA. A. BUCEK, Ann. pædiat. **177**:111 (Aug.) 1951.

A case of fibrinogenemia is described in a 12-year-old girl, with severe hemorrhagic diathesis combined with intermittent thrombopenia. The time of bleeding was unusually prolonged. There was no coagulation. Two brothers of the patient had bleeding from the umbilical cord after birth; one of them died shortly after birth, and the other died, when 3 years old, of intracranial hemorrhage after an accident. The parents and a brother have normal blood counts.

FROM THE AUTHOR'S SUMMARY.

IS SLIGHT ANEMIA IN THE CHILD A PHYSIOLOGICAL CONDITION? B. JASINSKI, Ann. pædiat. **177**:129 (Sept.) 1951.

From their investigations the authors were led to the conclusion that 50% of children are suffering from a masked deficiency of iron. Slight anemia neither in the mother nor in the child is physiological but is largely caused by lack of iron. The textbook statements that hemoglobin values between 75 and 95% are normal in children are erroneous. The low figures in otherwise healthy children are most certainly due to iron deficiency. Iron deficiency in children is caused probably less by food lacking in iron than by inability to utilize an amount of iron sufficient for the growing organism. The only rational measure to repair the iron deficiency of children effectively is treatment with easily assimilated and easily digestible iron salts.

FROM THE AUTHOR'S SUMMARY.

CONSTITUTIONAL PANMYELOPHTHISIS WITH MULTIPLE DEGENERATIONS. T. BAUMANN, Ann. pædiat. **177**:142 (Sept.) 1951.

A case of constitutional hereditary panmyelophthisis with Fanconi's syndrome is described in detail, and the clinical picture is discussed, with quotations from the world literature. With the help of a family tree, it is further shown that, in the same family, a heredopathological constitutional dysfunction of the active mesenchyma may manifest itself in the phenotype in four different clinical pictures, namely, in a simple granulocytopenia, in an acute agranulocytosis syndrome, in a panmyelopathia with Fanconi's syndrome, and in an acute myeloblastic leukemia.

FROM THE AUTHOR'S SUMMARY.

HEREDITY IN THE INFANTILE TYPE OF GAUCHER'S DISEASE. E. STRANSKY and T. L. CONCHU, Ann. pædiat. **177**:319 (Nov.) 1951.

A case of infantile Gaucher's disease (familial splenic anemia) in a 20-month-old girl is presented, with evidence of Gaucher's cells in the spleen, liver, and bone marrow. The father of the child harbored Gaucher's cells in the bone marrow but had no other symptoms. As this is the second case observed by one of the authors (E. S.), in which one parent has been the carrier of the disease, it is more than probable that the disease is inherited. One parent seems to be the carrier of the Gaucher trait, or the metabolic disorder leading to storage disease in its rudimentary form, which may develop in the next generation to manifest Gaucher's disease, either of the acute (infantile) or chronic (adult) type. It is hoped that further observations will elucidate the details of this inheritance, discovered by Groen.

FROM THE AUTHORS' SUMMARY.

ELECTROCARDIOGRAM CHANGES IN CHILDHOOD WITHOUT MYOCARDIAL DISEASE. W. FRISCHKNECHT, Helvet. paediat. acta **6**:443 (Nov.) 1951.

It is emphasized that even in childhood a diagnosis of myocardial disease is too frequently made on the basis of electrocardiographic changes alone. With the help of the orthostatic electrocardiogram, the electrocardiogram after "hydergine" or "dihydroergotamine" (dihydrogenated alkaloids of ergot), and the electrocardiogram after exercise, changes in the electrocardiogram due to neurovegetative influences can be recognized. The cerebral influence on the electrocardiogram is emphasized, as well as the influence of the position of the heart.

The hormonal and humoral factors which influence the electrocardiogram were explained by means of electrocardiograms in hypothyroidism, hypokalemia, and anemia.

The frequency of electrocardiographic changes in 2,000 infants and children in the Kinderspital Zurich was compared with that in 1,000 military pilots. The frequency of disturbances in the nodal points and in conduction was approximately the same in the two groups.

FROM THE AUTHOR'S SUMMARY.

BLOOD CHANGES AFTER TRANSFUSION IN MEDITERRANEAN ANEMIA. S. VIRDIS, Ann. ital. pediat. **3**:550 (Dec.) 1950.

The author reports upon the hematologic modifications (corpuscular value, osmotic corpuscular resistances, mean corpuscular diameter, Capp's reflex, and nucleated erythrocytes in the blood) caused by blood transfusions in four subjects, of whom three were affected by Mediterranean anemia (Cooley's type) and one by an attenuate form (Rietti-Greppi-Micheli's type).

FROM THE AUTHOR'S SUMMARY.

A CASE OF HAND-SCHÜLLER-CHRISTIAN DISEASE AND ITS POSSIBLE RELATION TO CORTICOSURRENAL DYSFUNCTION. R.CORDA, Ann. ital. pediat. **4**:431 (Oct.) 1951.

The author reports a case of Schüller-Christian disease in a 9-year-old girl, characterized by the presence of areas of osteoporosis in the diploë, by a slight monolateral exophthalmus, by high levels of cholesteremia, and finally by the presence of characteristic foam cells in the sternal marrow.

After a short review of the numerous theories on the etiopathogenetic explantation of this disease, starting from a theoretical view based upon the undoubted importance that the adrenals have in the metabolism of cholesterol, the author reports the therapeutic results obtained by the administration of synthetic adrenocorticotropic preparations in Schüller-Christian disease.

The particular and favorable evolution of clinical manifestations suggests that there is a relation between Schüller-Christian disease and the condition of corticosurrenal dysfunction.

FROM THE AUTHOR'S SUMMARY.

NEW DIAGNOSTIC AND THERAPEUTIC METHODS IN CONGENITAL CARDIOPATHY. GIUSEPPE FALCHI, Arch. ital. pediat. e puericolt. **13**:295, 1949.

The author emphasizes the great importance of the progress obtained by the introduction of heart catheterization in the diagnosis of cardiopathy, and he explains details of the technique.

He discusses the ether test and determination of the blood pressure within the cardiac cavities. The results of angiocardiography are reported, and some demonstrative roentgenograms are shown.

The oximetric method (technique, researches), which is such a valuable and practical aid in evaluating the preoperative conditions of heart patients, is described at length. Surgery of congenital cardiopathies is clearly explained, although some of the operative details of more interest to surgeons than to physicians are omitted.

Strict adherence to the technical rules is the best guarantee for the prophylaxis of thrombophlebitis. It should be emphasized that, although prudence is always to be recommended, the surgeon should not permit too great caution to prevent him from performing the operation if it is advisable.

FROM THE AUTHOR'S SUMMARY.

RUTIN IN CONDITIONS IN INFANTS WITH REDUCED CAPILLARY RESISTANCE. G. NICHELE and L. CARLINO, Arch. ital. pediat. e puericolt. **14**:351, 1951.

The authors studied the behavior of capillary resistance after treatment with rutin in 39 children with various diseases but with an increased fragility of the vessels. In 8 cases (20%) the vascular resistance had become normal, in 16 cases (41%) the resistance had notably improved, in 10 cases (26%) there was little improvement, and in 5 cases (13%) there was no change in the vascular resistance. The authors noted that the improvement was more obvious in tuberculous children treated with streptomycin, while no alterations were noted in the vascular fragility of children suffering from simple purpuras, and very slight improvement was observed in all other diseases.

FROM THE AUTHORS' SUMMARY.

PLATELETS AND BLOOD COAGULATION. F. FORTUNATO, Clin. pediat. **32**:521 (Oct.) 1950.

Three cases of purpura are reported in which there was prolongation of both coagulation and bleeding times. The delayed coagulation is attributed to pathology of the platelets, which appear to have a deficiency of thromboplastinogenase.

HIGGINS, Boston.

SIDEREMIA IN CHILDREN. M. LATO, Clin. pediat. **32**:561 (Oct.) 1950.

A review is given of the present knowledge as to the iron content of the blood of children.

HIGGINS, Boston.

ELECTROENCEPHALOGRAPHIC CHANGES AFTER ANGIOCARDIOGRAPHY AND AFTER SLOW INTRAVENOUS INJECTIONS OF THE CONTRAST MATERIAL USED FOR ANGIOCARDIOGRAPHY IN CHILDREN WITH NO HEART LESION. R. BULGARELLI and M. L. GROSSI BIANCHI, Lattante **22**:337 (June) 1951.

Two groups of children were studied, (1) those with congenital heart lesions undergoing angiocardiography, and (2) those with no heart or brain lesion who received slow intravenous injections (15 seconds) of one of the drugs used in angiocardiography. The electroencephalograms of the children in both groups showed abnormalities, which were more marked in the cases of the children with heart lesions. These abnormalities disappeared rapidly. The drugs are believed to affect the brain tissue, probably by vasomotor vascular reactions in the cerebral vessels and by permeability of the capillaries, and possibly by osmotic changes in the blood.

HIGGINS, Boston.

FRAGILITY OF RED BLOOD CELLS IN THALASSEMIA (COOLEY'S ANEMIA). P. TOLENTINO and V. GALLO, Minerva pediat. **2**:584 (Dec.) 1950.

Although the mean fragility of the red blood cells in patients with thalassemia (Cooley's anemia) is no different from that of normal children, the variability from the mean of the individual cells is much greater.

HIGGINS, Boston.

FIRST STUDIES ON TRANSVERSE AXIAL, ASSOCIATED WITH FRONTAL, STRATIGRAPHY IN ACQUIRED RHEUMATIC HEART DISEASE. R. BULGARELLI and L. OLIVA, Minerva pediat. **3**:311 (June) 1951.

The shadows obtained by stratigraphy afford a useful means of studying the dimensions of each of the four chambers of the rheumatic heart.

HIGGINS, Boston.

THE HEART OF THE GROWING CHILD AND THE SYNDROME OF CARDIAC INEFFICIENCY. G. GRANATA, Minerva pediat. **3**:375 (July) 1951.

Two types of cardiac insufficiency without organic defect are to be found in the growing child. In one type there is an enlarged heart, which is still unable to meet the demands of bodily exercise. In the other type the heart is not enlarged and does not meet the demands of the body in stress; this type is usually called the effort syndrome of Lewis. Both these types really belong in the same category, which the author chooses to call the inefficient growing heart (*coeur inefficient de la croissance*).

HIGGINS, Boston.

LYSOZYME IN CHILDREN. E. HOLZKNECHT and G. POLI, Minerva pediat. **3**:380 (July) 1951.

Determinations are reported of the lysozymatic activity of the blood sera, the tears, and the saliva of infants and children of various ages. The activity is greater in the blood and secretions of breast-fed than of bottle-fed infants and in general is higher in well-nourished than in poorly nourished children. No lysozymatic activity could be found in the urine or in the cerebrospinal fluid.

HIGGINS, Boston.

HEMORRHAGIC SYNDROME DUE TO ANTICOAGULANTS IN THE CIRCULATION FROM BIRTH. M. CRISALLI and G. COTELLESSA, Minerva pediat. **3**:441 (Aug.) 1951.

A boy of 10 years was in general good health, and no family history of bleeding was elicited. He had had a hemorrhage from the umbilicus at birth and a hemarthrosis at 14 months. Since that time he has had frequent ecchymoses and bleeding episodes. His blood coagulation time was 60 to 180 minutes but fell to 15 to 20 minutes after an intravenous injection of toluidine blue. This appears to be the first case in the literature of a patient with a hemorrhagic disease due to a circulating anticoagulant present at birth.

HIGGINS, Boston.

RIGHT ANTERIOR AORTIC ARCH ASSOCIATED WITH TETRALOGY OF FALLOT. R. BULGARELLI, Pediatria **57**:729 (Sept.) 1949.

A case is reported of a right anterior aortic arch and tetralogy of Fallot in a boy of 4 years. The diagnosis was established with the help of an angiocardiogram and esophagogram. The angiocardiographic findings in various abnormalities of the aortic arch and its branches are discussed.

HIGGINS, Boston.

PURULENT PERICARDITIS CURED BY PENICILLIN INTRAPERICARDIALLY. G. ACETO, Pediatria **59**:383 (May) 1951.

A child of 14 months had had a pneumococcic pericarditis, which had not responded to intramuscular injections of penicillin. Over a period of four days, aspiration of pus from the pericardium was followed by intrapericardial injections of 200,000, 400,000, and 600,000 units of penicillin, each in 10 cc. of isotonic sodium chloride solution. The child recovered, his fever falling by crisis following the second injection.

HIGGINS, Boston.

CONSTITUTIONAL HEREDITARY THROMBOCYTOPENIA OF THE WILLEBRAND-JUERGENS TYPE. F. PECORELLA and S. PULEJO, Pediatria **59**:549 (July) 1951.

A report is given of a 9-month-old child with episodes of bleeding and purpura since the age of 4 months. The blood platelets were few in number and usually appeared singly in the blood smears. Marrow smears showed only a few megakaryocytes.

HIGGINS, Boston.

TWO INSTANCES IN WHICH JAKSCH-HAYEM-LUZET ANEMIA OCCURRED IN ONLY ONE OF FRATERNAL TWINS. M. SAGGESE and G. CROCCO, Pediatria **59**:565 (July) 1951.

Two cases of Jaksch-Hayem-Luzet anemia (infantum pseudoleukemia) are reported. In each case there was a fraternal twin who was healthy and had a normal blood picture.

HIGGINS, Boston.

CASE OF INFECTIOUS MONONUCLEOSIS WITH ATYPICAL COURSE IN A BOY OF 6 YEARS. ROANO ROSSI and ALFREDO LOTTINI, Riv. clin. pediat. **48**:773 (Dec.) 1950.

A case of infectious mononucleosis with leukemoid reaction is described. The authors reexamine the mechanism regulating medullary maturation and proliferation, also taking into account the possible interrelations existing between mononucleosis and leukemia, especially in the light of the most recent concepts of infection.

FROM THE AUTHORS' SUMMARY.

SURGERY OF HEART DISEASES. PEDRO RODRIGUEZ DE LEDESMA, Acta pediat. españ. **8**:999 (Sept.) 1950.

Ledesma, who spent eight months in the United States studying in medical centers where heart surgery is done, gives in this report details of diagnosis and technique in the various forms of congenital heart disease amenable to surgical treatment. The reason for the article is the scarcity of literature available in the Spanish language dealing with these conditions.

He divides his article into (1) common types of congenital anomalies, with illustrations and photographs of each type; (2) details of examination, history, and roentgenologic findings to aid in diagnosis of various forms of heart lesions, and the formula for estimating the flow of oxygenated blood in the large vessels and through the heart, and (3) details of surgical treatment of coarctation of the aorta, persistent ductus arteriosus, tetralogy of Fallot, and mitral stenosis.

ALLEN, Santa Fe, N. M.

SOCIAL AND EPIDEMIOLOGICAL STUDY OF CARDIOPATHIES, WITH SPECIAL REFERENCE TO CONGENITAL HEART DISEASE. MEGIAS VELASCO, Acta pediat españ. **9**:807 (July) 1951.

Velasco studied the results of mass roentgenologic examination of school children, and from those showing heart abnormalities he made a study of heart lesions. Among 245 cardiac lesions studied with further roentgenograms, electrocardiograms, etc., he found certain families in which rheumatic fever was recurrent among the school children. The need to control rheumatic fever is obligatory, he says, to any heart program. Many of these lesions not actually crippling in childhood will be disabling in adulthood. Previously, congenital lesions were not amenable to treatment, but now, whenever possible and advisable, they should be treated by appropriate surgery. Cases should be carefully selected.

Case histories, photographs, and illustrations are given. There is also a discussion of the clinical diagnosis of cardiopathies with differentiation between rheumatic and congenital forms.

The author feels that there should be much postgraduate work for doctors in order that they may become reoriented in the matter of the prevention and treatment, as well as in the diagnosis, of heart lesions in children.

ALLEN, San Francisco.

CARDIAC CATHETERIZATION IN NORMAL CHILDREN. R. SCHIFFRIN O., Rev. chilena pediat. **21**:259 (June) 1950.

The importance and the different techniques of heart catheterization are mentioned. The author describes the method used by him in 15 normal children. In 10 of them he used the cephalic vein to introduce the catheter, while in the remaining five he utilized the saphenous vein. He describes the roentgenologic study of the course of the catheter in the different heart chambers. The author also studied the intracardiac pressure recordings of the right-sided chambers and their relations to the simultaneous phonocardiographic findings. The intracardiac pressure was also studied by means of a water manometer.

FROM THE AUTHOR'S SUMMARY.

OSTIUM ATRIOVENTRICULARE COMMUNE. OTTO GARCIA, Rev. cubana pediat. **22**:451 (Aug.) 1950.

Ostium atrioventriculare commune in an 8-year-old girl is reported. The case is interesting because of the exhaustive study made during life. The importance of the study of pulmonary shadows simulating tuberculosis in children with congenital heart disease is emphasized.

FROM THE AUTHOR'S SUMMARY.

A CASE OF SICKLE CELL ANEMIA OR DREPANOCYTEMIA. JORGE MUNOZ TURNBULL and RUBEN LAVALLE ARGUDIN, Bol. méd. Hosp. inf., México **7**:3 (Feb.) 1950.

The authors present a case of sickle cell anemia, or drepanocytemia, which is very rare in Mexico. This is the second case seen in the Hospital Infantil. This disease seems to be confined almost entirely to Negroes but a few cases have been observed in white persons, especially those of Greek, Italian, Spanish, and Mexican background. Clinically, it is characterized by symptoms of anemia, rheumatic manifestations, acute attacks of abdominal pain, ulcers of the legs, and neurologic signs, such as somnolence, coma, hemiplegia, aphasia, convulsions, headache, stiffness of the neck, nystagmus, and transitory or permanent blindness. Not all of these signs were present in the patient. Hematologically, in this anemia, the red blood cells are found to acquire a sickle-like or crescent shape, and there are signs of excessive cell destruction and of active regeneration. In the patient under study, the authors found some characteristic data which made possible the diagnosis; these were morphologic changes of the cells under tension of $CO_2$, anemia with symptoms of active hematic regeneration, the leucocytosis, and bilirubinemia.

The authors speculate on the differential diagnosis with other diseases, such as familial hemolytic anemia. Also, differentiations are made between sickle and elliptic cells.

FROM THE AUTHORS' SUMMARY.

A CASE OF CONSTRUCTIVE PERICARDITIS TREATED WITH DECORTICATION. TOMAS F. GONDA and ANTONIO TORRES D. ANDA, Bol. méd. Hosp. inf., México **7**:538 (Aug.) 1950.

The authors report a case of constructive pericarditis in which a successful decortication was performed.

FROM THE AUTHORS' SUMMARY.

DIFFERENTIAL DIAGNOSIS OF MORBUS CAERULEUS. A. SCHAEDE, Deutsche med. Wchnschr. **75**:1681 (Dec. 15) 1950.

Fifty-five per cent of 160 congenital heart lesions seen in one year belonged to the tetralogy-of-Fallot group. The paper discusses briefly the differential diagnosis of morbus caeruleus, with special reference to indications for surgery. Some very good illustrations are given.

AMBERG, Rochester, Minn.

ETIOLOGY AND THERAPY OF GOAT MILK ANEMIA. KLAUS BETKE and LOTHAR GANTERT, Deutsche med. Wchnschr. **76**:1341 (Oct. 26) 1951.

The term, "goat milk anemia," is used to mean that anemia which occurs with nutrition by goat's milk, presenting a megalocytic blood condition and a megaloblastic bone marrow. It is admitted that iron-deficiency anemia also can occur with goat's-milk feeding. Two cases are reported, both in dystrophic infants. Both infants were cured by the administration of folic acid and vitamin B complex.

AMBERG, Rochester, Minn.

HEART LESION IN PRIMARILY CHRONIC RHEUMATIC ARTHRITIS. SCHNELLER, Med. Klin. **45**:271 (March 3) 1950.

Of 100 patients with primarily chronic rheumatic arthritis, 36 presented an electrocardiogram indicating myocardial lesion. The number of patients showing such lesion increased with the severity of the rheumatic arthritis. No valvular lesions were seen.

AMBERG, Rochester, Minn.

HYPERSPLENISM IN CHILDREN. J. JANELE, Pediat. listy **5**:301, 1951.

The author gives an account of two children (7 and 10 years old) with secondary hypersplenism (congenital hemolytic jaundice, splenomegalic hepatic cirrhosis), three children (4½ and 10 years old) with hypersplenism in Banti's syndrome, and one boy (13 years old) with primary splenic pancytopenia. In all the children splenectomy was performed, combined in some cases with anastomosis of the splenic and renal veins. The operations were successful; the blood findings, as well as the general state of health, improved.

FROM THE AUTHOR'S SUMMARY.

POSTMORTEM FINDINGS OF CONGENITAL MALFORMATIONS OF THE HEART AT THE FIRST PATHOLOGICOANATOMICAL INSTITUTE IN 1945-1949. H. SIKL, Pediat. listy **6**:15, 1951.

During the five-year period, 1945-1949, among 8,624 autopsies 228 cases of congenital malformation of the heart were found. This is 2.65%. Minor variations, such as in the number of the semilunar valves, were not counted. Only 32 patients lived to be more than 1 year old and 22 lived to be over 10. Surgical treatment could have been considered in seven cases; in three there was persistent ductus arteriosus and in four tetralogy of Fallot. Concerning three cases of anomalous pulmonary veins, a separate report will be given by Dr. Benesova.

FROM THE AUTHOR'S SUMMARY.

EXPERIENCE WITH SURGICAL TREATMENT OF PATENT DUCTUS ARTERIOSUS. E. POLAK, H. PADOVCOVA, and I. BOR, Pediat. listy **6**:23, 1951.

Eight patients with patent ductus arteriosus who were operated upon at the Vinohrady Hospital, Prague, are reported upon. The first operation was performed in 1946, at a time when the surgical department had not yet been equipped with apparatus for intratracheal narcosis. The patient had myocarditis with decompensation, was in a very bad general condition, and subsequently died. The remaining seven patients, operated upon under modern anesthetic conditions, all recovered without complications. Frontal thoracotomy was performed in all cases. Obliteration of the duct was accomplished either by two borderline ligatures and injection of a dextrose solution into the duct between these, or else by suture. In all seven cases the continuous murmur caused by the patent duct disappeared immediately after operation, and in no case did it reappear.

FROM THE AUTHORS' SUMMARY.

CLINICAL FEATURES AND DIAGNOSIS OF INFECTIOUS MONONUCLEOSIS. V. KREDBA and J. ONDRACEK, Pediat. listy **6**:137, 1951.

On the basis of their observations of 143 children with infectious mononucleosis (during three and one-fourth years) the authors describe the clinical picture of the disease. The disease can take an acute course, with findings in the throat, swelling of the lymph nodes, and enlargement of the spleen and the liver. The spleen and the liver are enlarged only in some cases. In the subacute form of the disease the onset is insidious. First one can observe enlargement of the lymph nodes of the neck, and a periglandular edema develops; then the spleen and the liver enlarges, and only then does the patient complain of sore throat, while a follicular or necrotic angina develops. The disease can be distinguished from diphtheria by the findings in the throat, although the finding on the lymph node looks threatening, as in the malignant form of diphtheria. Enlargement of the spleen and liver, as well as of other groups of lymph nodes, is the rule. Seldom does mononucleosis take a chronic course. The patient complains for months of weakness and pain in the limbs, has an increased temperature in the afternoon, and exhibits hepatosplenomegaly.

For diagnosis the most important factor is the blood picture, with a leucocyte count of 10,000 to 20,000 and an increase of the number of mononuclear cells to 70 to 90%. There is an increase in the number of normal lymphocytes, large lymphocytes, monocytes, and plasmatic cells and an increase of the lymphoid monocytes typical of mononucleosis. The proportion of the latter reaches 5 to 30% of the white cells.

The prognosis is good. There is a danger of rupture of the spleen or paralysis of the breathing center. The acute form subsides within a few days, the subacute form in two to three weeks. Penicillin has a beneficial effect; the sore throat disappears within two to four days, and the temperature decreases.

GRULEE, Evanston, Ill.

PRIMARY REFRACTORY ANEMIA IN CHILDHOOD. J. JANELE, Pediat. listy **6**:151, 1951.

Within the last five years six cases of this rare illness have been observed in children 1, 2, 3, and 6 years old. Four children probably had Fanconi's syndrome of anemia coupled with degenerative symptoms and retardation of psychic development. In two cases the development was within normal limits. In one case the mother of the child also had anemia, and anamnestic data suggested two further cases among other members of the family in three generations.

GRULEE, Evanston, Ill.

MYELOBLASTIC LEUKEMIA. BENT MOLLER, Acta pædiat. **37**:492, 1949.

Two cases of acute myeloblastic leukemia are described and discussed. The first, in a boy aged 3 years, was a panmyelophthisis of unknown origin (verified by bone marrow examination), severe anemia, granulocytopenia, and thrombocytopenia. After treatment with blood transfusion and penicillin, and later with liver injection, folic acid, and iron compound, a complete remission, with normal regeneration of the bone marrow, took place. Two weeks later a fulminating myeloblastic leukemia developed, and a week later the boy died as a result of internal hemorrhage after puncture of the spleen. Autopsy showed pronounced hepatosplenomegaly and universal myeloblastic infiltration.

The second case was that of a boy aged 14 in whom acute myeloblastic leukemia developed, giving rise initially to neurologic symptoms only: transitory paresis of the eye muscles and paresthesia corresponding to the trigeminal nerves. During treatment with urethan, liver extract, and folic acid, greater differentiation occurred in the bone marrow and in the peripheral blood; a decrease in the leucocyte count and a transitory clinical improvement were also noticed. Fifty days after the first appearance of the symptoms the patient died of hemorrhagic anemia and sepsis.

FROM THE AUTHOR'S SUMMARY.

FAMILIAL HEMORRHAGIC DIATHESES WITH PROLONGED BLEEDING TIME (PSEUDOHEMOPHILIA, THROMBOPATHIES). OLGA IMERSLUND, Acta pædiat. **38**:311, 1949.

The author has studied clinical manifestations and hereditary conditions in 22 patients suffering from chronic hemorrhagic diathesis with the same features as those described by von Willebrand: prolonged bleeding time, usually a normal number of thrombocytes, and normal coagulation time. The author has found nothing to show that the tendency to bleed is due to so-called thrombopathy. The results of the investigation of hereditary conditions suggest the existence of at least two different hereditary types, one with a recessive factor and the other with a dominant factor inherited.

FROM THE AUTHOR'S SUMMARY.

DISAPPEARANCE OF RHEUMATIC CARDITIS AND DELAYED APPEARANCE OF RHEUMATIC HEART DISEASE. ERIK JACOBSSON, Acta pædiat. **38**:324, 1949.

In a follow-up examination of patients who had rheumatic fever during childhood, the author studied in particular the disappearance of the rheumatic carditis, as well as the likelihood of the delayed appearance of heart damage. He has found that the risk of permanent cardiac disorder developing in connection with rheumatic fever increases in proportion to the severity of the initial carditis. The initial carditis, however, may clear up so completely that no permanent cardiac affection can be detected at later examination. Even though during an attack of rheumatic fever the heart may be completely, or almost completely, free of carditis, a valvular lesion may nevertheless develop at a later stage.

FROM THE AUTHOR'S SUMMARY.

DOES CHOREA CAUSE CARDITIS? BERNHARD LANDTMAN, Acta pædiat. **38**:377, 1949.

A study of 18 children in their initial attack of chorea is presented. Only two of these showed evidence of carditis, and both of them had had other rheumatic manifestations. The possibility of multiple origin for chorea is discussed. FROM THE AUTHOR'S SUMMARY.

ACUTE INFECTIOUS LYMPHOCYTOSIS. H. GLASTRUP, Ugesk. læger **112**:1214 (Aug. 31) 1950.

A report is presented of three cases of acute infectious lymphocytosis in Danish children, twins 11 months old, and a 6-month-old infant. The third child was hospitalized for social reasons in the same ward as the first child. The children displayed signs of slight infection. They had leucocytosis: white cell count 27,800 to 15,700, with 85 to 77% lymphocytes. The bone marrow in all three cases did not show any abnormal cells; the lymphocyte content was increased. The children recovered.

WALLGREN, Stockholm, Sweden.

INVESTIGATIONS ON A CIRCULATING ANTICOAGULANS IN A HEMOPHILIAC. S. VAN CREVELD, M. M. P. PAULSSEN, and P. G. HOORWEG, Nederl. tijdschr. geneesk. **94**:1833 (July 1), 1950.

Report is made of a number of investigations performed on a hemophiliac who became refractory to treatment with either fresh whole blood, plasma, or plasma fractions. The refractoriness appeared to be due to the presence of a circulating anticoagulant. Fractionation of the plasma was carried out, and it was found that the anticoagulant was associated with the pseudoglobulin fraction of plasma. The mechanism of the action of the anticoagulant was the inhibition of the action of the antihemophilic globulin (coagulation globulin). The antihemophilic globulin was not altered by the anticoagulant and could be reprecipitated without loss of its antihemophilic properties.

The anticoagulant was shown not to inhibit prothrombin, thromboplastin, and fibrinogen. It was also demonstrated that this anticoagulant was related neither to the lipid antithromboplastin nor to heparin.

VAN CREVELD, Amsterdam, Netherlands.

INFLUENCE OF ADMINISTRATION OF DEXTROSE UPON THE POTASSIUM CONTENT OF THE BLOOD SERUM IN NORMAL PERSONS AND NONDIABETIC PATIENTS. J. GROEN, A. F. WILLEBRANDS, C. E. KAMMINGA, H. K. VAN SCHOTHORST, and E. C. GODFRIED, Nederl. tijdschr. geneesk. **94**:2187 (July 29) 1950.

In a former article the authors found that during treatment with large amounts of insulin the potassium content of the serum decreased in a high degree, and less potassium was excreted in the urine. Under these circumstances potassium shifted from the extracellular to the intracellular space. This was apparently caused by the insulin. In the present article the authors report upon the extent to which this potassium shift can be demonstrated in normal persons and in nondiabetic patients, who were first given a potassium-free diet for two days and then, in the course of two of three hours, either 100 to 180 gm. of dextrose intravenously or a meal rich in carbohydrates. The potassium content of the serum in the normal persons decreased and reached a minimum after 6 to 9 hours. If the administration of dextrose was continued for days, changes in the electrocardiograms were also noted, namely, a decrease of the T wave and prolongation of the Q-T interval. Together with the hypopotassemia, a decrease of the inorganic phosphate was noted. One is dealing here with a physiological phenomenon, occurring when dextrose, by the action of the insulin, is deposited in the muscles.

VAN CREVELD, Amsterdam, Netherlands.

RESULTS OF OPERATIVE TREATMENT IN 12 PATIENTS WITH COARCTATION OF THE AORTA. I. GOEREMA, Nederl. tijdschr. geneesk. **94**:2394 (Aug. 19) 1950.

Report is made of 12 patients operated upon for coarctation of the aorta. Because of the risk, the indication for operation is much more difficult than in patent ductus arteriosus.

In 10 of these patients, resection of the stenosed part of the aorta had a good result. In one patient, a 21-year-old man, resection was impossible because of severe arteriosclerosis. One patient died. He, too, had arteriosclerosis, and the aorta wall ruptured four days after the operation.

The decision for operative treatment is still difficult. Three patients died without operation (respectively 21, 17, and 5 year old) from heart failure, aortic rupture, and bacterial endocarditis. None of them had complaints until a short time before death. After this unfortunate experience, two patients, both women 18 years old, both without complaints, were operated upon preventively with complete success. Nevertheless, it is at present not advisable to operate upon all patients with coarctation preventively.

VAN CREVELD, Amsterdam, Netherlands.

## Diseases of Nose, Throat, and Ear

HISTOPATHOLOGY OF LATENT OTOANTRITIS IN THE INFANT. P. GIRARDET and J. P. CHRISTEN, Helvet. pædiat. acta **6**:71 (Feb.) 1951.

The work is based upon 176 histological examinations of the petrous portion of the temporal bone of 93 newborn infants, infants, and small children who died of various diseases. The anatomical peculiarities of the middle ear and of its accessory cavities are explained by means of serial sections and roentgenological study after injections with iodized oil (lipiodol®). The authors discuss the term latent otoantritis which seems to define best the clinical picture and the alterations observed. They make the following conclusions.

1. Latent otoantritis is a typical illness of newborn and young infant. It is found particularly often, by section, in infants aged 1 to 4 months old and less often in infants older than 7 months. In the second age group acute otomastoiditis is much more frequent. In small children latent otoantritis is rarely found.

2. Generally there are no perceptible clinical symptoms. From the histopathological point of view it is difficult to determine the clinical importance of the illness; it is characterized by relatively small lesions. The authors never observed collections of pus or necrosis of bones.

3. Latent otoantritis is not necessarily connected with dystrophy, since it is nearly as frequent in sthenic and newborn infants as in weak children. It depends chiefly upon the age of the patient. The special pathology of the upper respiratory tract of the young infant explains this fact, and the authors show the analogy between the pathogenesis of latent otoantritis and that of immature pneumonias in the first months of life. The topography of the Eustachian tube, the middle ear, and the antrum, the hospital surroundings, and the horizontal position of the infant during his meals are additional pathogenetic factors.

4. Latent otoantritis is nearly as frequent among infants without digestive disturbances as in infants suffering from such troubles. On the other hand, the latter show a higher proportion of severe and average lesions. No lesions have been found, however, which were so serious that they called for antrotomy.

FROM THE AUTHORS' SUMMARY.

MAXILLARY SINUSITIS AND THE POSTSINUSITIC LUNG SYNDROME IN ROENTGENOLOGIC PRACTICE. H. H. WEBER, Schweiz. med. Wchnschr. **81**:207 (March 3) 1951.

In cases of chronic cough, particularly in children, thickening or shadowing of one or both maxillary sinuses was seen in about 25% of the cases.

AMBERG, Rochester, Minn.

RADIOTHERAPY OF ADENOIDS IN INFANTS. R. CLEMENT and R. BOURDON, Lattante **20**:577 (Oct.) 1949.

The technique of irradiation of enlarged and/or infected tonsils and adenoids by x-rays and by radium is discussed. In the past 23 years at the Bretonneau Hospital in Paris, irradiation of tonsils and adenoids has resulted in satisfactory results in 66% of the cases and was of no benefit in 6%. In 27%, there was functional improvement of the patient, although the adenoid and tonsillar tissues remained hypertrophied.

HIGGINS, Boston.

CLINICAL AND SURGICAL ASPECTS OF LATENT, OR UNRECOGNIZED, OTITIS IN INFANTS. T. E. ROSSI and G. BELLIENI, Minerva pediat. **3**:224 (April) 1951.

Unrecognized nonsuppurative otitis may be the causative factor of severe toxic enteric disorders. The diagnosis is difficult. The pathology, clinical symptoms, diagnosis, and treatment are discussed.

HIGGINS, Boston.

ACUTE RHINITIS IN SCHOOL CHILDREN. S. GARCIA VICENTE, Acta pediat. españ. **9**:606 (May) 1951.

The author discusses the benefits of discovering cases of acute rhinitis before the sinuses are affected. There have been especially good results in the treatment of atrophic rhinitis before it develops into ozena which is difficult to treat effectively.

ALLEN, San Francisco.

INDICATIONS FOR TONSILLECTOMIES IN PEDIATRICS. ANTONIO PRADO VERTIZ, Acta pediat. españ. **9**:686 (June) 1951.

This excellent appraisal of the indications for tonsillectomies is based on a study of more than 6,000 children upon whom operations were performed at Children's Hospital, México, D. F., in comparison to children with similar complaints who were not subjected to operation.

The author lists 12 supposedly valid reasons for tonsillectomies and rejects most of them. These indications are (1) local infection, (2) chronic hypertrophy, (3) recurrent tonsillitis, (4) frequent rhinitis, (5) otitis media and deafness, (6) prevention of infection in Waldeyer's tonsillar ring, (7) rheumatic fever, (8) prevention of other arthritic conditions, (9) nephropathies, (10) allergic diseases, (11) prevention of other acute infections, and (12) social reasons, such as mouth breathing and bad breath.

Vertiz concludes that unless the tonsillar tissue is actually diseased the tonsils should be retained as the first line of defense in childhood. Most of the reasons formerly held to be valid for removing tonsils, in early childhood at least, are shown statistically to be inadequate.

ALLEN, San Francisco.

ADVANCES IN TREATMENT OF CROUP IN CHILDREN. A. WINDORFER, Deutsche med. Wchnschr. **75**:923 (July 14) 1950.

Croup due to unspecific micro-organisms such as those seen in influenza, measles, scarlet fever, and pertussis, as well as croup due to diphtheria, may be cured by early treatment with penicillin. In all cases diphtheria antiserum and penicillin are given as early as possible. All of the 68 patients in this study could be cured. By this method of treatment mortality can be reduced further.

AMBERG, Rochester, Minn.

INDICATIONS FOR TONSILLECTOMY IN CHILDREN. B. WISKOVSKY, Pediat. listy **6**:8, 1951.

The following circumstances are listed as indications for tonsillectomy in children: (1) frequent recurrence of follicular (not catarrhal) tonsillitis, if it is not brought about by a high exposure to infection (mouth breathing, hemolytic Streptococcus carriers in the child's environment); (2) protracted severe tonsillitis with unsatisfactory convalescence or with relapse within a short time (2 to 3 weeks); (3) protracted peritonsillar abscess; (4) in cases lacking a history of tonsillitis, only if the tonsils are hypertrophic to such an extent that they cause substantial limitation of the pharyngeal passage, or in the presence of signs of chronic tonsillitis (frequent formation of spots on the tonsils, stagnation of these spots, foul-smelling contents in the tonsillar follicles, peritonsillar adhesions, tonsils of unequal size, conditions after tonsillotomy); (5) diseases resulting from septic foci, with a positive tonsillar history or with signs of chronic tonsillitis, and (6) exceptionally, in cases with a normal tonsillar history and normal findings, if other infectious foci have been excluded by a thorough investigation.

FROM THE AUTHOR'S SUMMARY.

RADIUM IRRADIATION IN EFFECTIVE TREATMENT IN INFECTIONS OF THE NOSE AND THROAT IN CHILDREN. H. A. E. VAN DISHOECK, Maandschr. kindergeneesk. **19**:241 (Sept.) 1951.

Radium irradiation is an effective treatment for infectious foci in the nasopharynx causing tubotympanal catarrh. The principal consideration is combating the infection and not the removal of a supposed mechanical obstruction of the tubal orifice by adenoid tissue. Tonal dips or high-tone loss are not influenced by this therapy.

FROM THE AUTHOR'S SUMMARY.

## Diseases of Lungs, Pleura and Mediastinum

INCIDENCE OF MYCOTIC INFECTIONS IN CHILDREN WITH ACUTE RESPIRATORY DISEASE. F. C. WHITCOMB, A. MILZER, and R. H. KUNSTADTER, J. Pediat. **35**:715 (Dec.) 1949.

The authors discuss the routine skin testing of 211 children. Tests with histoplasmin, blastomycin, coccidioidin, and tuberculin were performed. Three cases of proved fungous infection are described: a histoplasmosis, a Candida albicans infection of the lung, and a fatal infection with an unidentified fungus.

MACDONALD, Pittsburgh.

PULMONARY INFILTRATION AND BLOOD EOSINOPHILIA IN CHILDREN (LOEFFLER'S SYNDROME). ROSA LEE NEMIR, ARTHUR HEYMAN, and J. D. GORVOY, J. Pediat. **37**:819 (Dec.) 1950.

Eight cases of Löffler's syndrome are reported. Seven patients had intestinal parasites which apparently provided the provocative allergen. The one patient who had no intestinal parasites had infected sinuses and, possibly, a bacterial allergy.

MACDONALD, Pittsburgh.

TERRAMYCIN IN TREATMENT OF PNEUMONIAS OF CHILDHOOD. CLINTON H. WOODING JR. and ROLAND B. SCOTT, J. Pediat. **38**:423 (April) 1951.

Ten children with pneumonia were treated with terramycin. The associated organisms varied and included pneumococci, streptococci, staphylococci, and Hemophilus pertussis. Nine children recovered in a reasonable time. One child tolerated the drug poorly but recovered with penicillin therapy.

MACDONALD, Pittsburgh.

A TREATMENT PROGRAM FOR CHRONIC CHILDHOOD SINOBRONCHITIS. WALTER C. PRICE and VERONICA B. BINNS, J. Pediat. **38**:597 (April) 1951.

A comparative study of treatment of 54 children with chronic sinobronchial infection is presented. Roentgenograms of the sinuses before, during, and after treatment were the criteria. The authors conclude that penicillin used parenterally and intranasally (aerosol), in conjunction with penicillin nose drops ("paradrine") and oral administration of methapyrilene (syrup of histadyl®), gives fair to excellent improvement in 95% of cases. The nose drops should precede the penicillin aerosol to open the air-ways.

MACDONALD, Pittsburgh.

OBSTRUCTIVE EMPHYSEMA WITH A DEFECT OF THE ANTERIOR MEDIASTINUM. JAMES E. LEWIS and WILLIS J. POTTS, J. Thoracic Surg. **21**:438 (May) 1951.

Anterior mediastinal openings with direct communication of right and left pleural cavities constitute an exceedingly rare group of congenital abnormalities. Only three proved cases of this type appear in the literature. Because of the anterior position of the right middle lobe in the right chest cavity, this lobe is apt to herniate through such an anterior mediastinal defect. Should this occur, obstructive emphysema of the right middle lobe results, due to torsion on the bronchus.

The authors report the case of a 4-month-old boy, admitted to Children's Memorial Hospital, Chicago, because of dyspnea and cyanosis with crying of six weeks' duration. Physical examination showed a mediastinal shift to the left side and hyperresonance to percussion over the right anterior side of the chest. Roentgenograms of the chest showed emphysema of the right middle lobe and atelectasis of the right upper and lower lobes. The heart was shifted to the left side. Resection of the right middle lobe was carried out. Closure of the anterior mediastinal defect was felt to be desirable but not advisable because of the precarious physical condition of the infant. The postoperative course was uneventful.

MEYER, Chicago.

RHEUMATIC PNEUMONIA. ROBERT B. TUDOR and ROBERT R. KLING, Minnesota Med. **34**:437 (May) 1951.

The authors report a case of rheumatic heart disease which terminated in a fulminating pulmonary lesion. They have collected eight similar cases from the literature. The exact origin of

this pneumonitis is not known, but it is similar to the pulmonary histopathology seen in experimental and sulfonamide anaphylactic pneumonitis. The authors theorized that this acute fulminating exudative pneumonia was rheumatic in origin.

STOESSER, Minneapolis.

ASTHMA IN CHILDREN. AVERY L. COTTON, New Orleans M. & S. J. **103**:524 (June) 1951.

The author calls attention to the importance of early and proper treatment of asthma in children. Desensitization and avoidance of allergies are primary considerations in children. Aminophylline is considered dangerous for children.

MCGUIGAN, Evanston, Ill.

THE BRONCHI DURING A CRISIS OF ASTHMA. P. VALLERY-RADOT, B.-N. HALPERN, J.-M. DUBOIS DE MONTREYNAUD, and V. PEAN, Presse méd. **58**:661 (June 14) 1950.

The mechanism of dyspnea during an asthmatic attack has not been sufficiently explained. The authors conducted a study of the changes occurring during artificially produced asthma and during clinical attacks of asthma. Guinea pigs, sensitized to crystalline egg albumin, were the subjects of the experimental study. By introduction of an aerosol mist of egg-albumin solution into the bronchi, an intense reaction was produced, with anaphylactic death within a few minutes. Normal guinea pigs were used in another series, and an aerosol mist of histamine solution was introduced. This procedure resulted in death within a few minutes.

Bronchoscopic examinations were carried out on patients before, during, and after attacks of asthma. Tetracaine hydrochloride ("pontocaine") anesthesia was used, without epinephrine. Biopsies of the bronchial mucosa were performed. From the studies, which are well illustrated in the article, the authors conclude that in allergic asthma the primary mechanism is an intense bronchial edema in conjunction with the generalized antigen-antibody reaction, while in nonallergic asthma this edema is not seen, bronchial spasm and hypersecretion of mucus producing the reaction instead.

DAFFINEE, Melrose, Mass.

A CASE OF UNILATERAL RECURRENT LUNG ATELECTASIS. IHSAN HILMI ALANTAR, Helvet. paediat. acta **4**:546 (Dec.) 1949.

In an 11-month-old infant being treated for an influenzal infection, a unilateral lung atelectasis was observed which disappeared completely at the end of 24 hours. One week later, concomitant with the beginning of serum sickness, the child suffered a new attack. On this occasion, the atelectasis disappeared gradually only after several days.

FROM THE AUTHOR'S SUMMARY.

CLINICAL, ROENTGENOLOGICAL, AND HEMATOLOGIC ASPECTS OF RESPIRATORY VIRUS INFECTIONS IN BABIES. ANTONIO PERRA, Ann. ital. pediat. **4**:115 (April) 1951.

The clinical, roentgenographic, and hematologic features of 29 patients with acute respiratory diseases observed in the Children's Clinic of Cagliari are described, and the cases are classified as virus pneumonia. The most frequent features of the disease are as follows: rapid but gradual onset, with fatigue, anorexia, and catarrhal or dry cough; irregular and rarely much-elevated fever which falls rapidly, and limited respiratory findings, with various localizations of congestion or infiltration areas. Roentgenographic examination reveals hilar shadows which widen to the periphery or, more frequently, downward. There is remarkable and frequent involvement of the cardiocirculatory system. Leucopenia or a leucocytosis was present in all cases, with polymorphonucleosis or lymphocytosis in almost as many cases. The prognosis in the great majority of cases is excellent. There is a possibility of severe infection, but this is rare.

FROM THE AUTHOR'S SUMMARY.

SULFONAMIDE THERAPY IN DISEASES OF THE RESPIRATORY TRACT IN CHILDREN. LUISA NORBIATO, Clin. pediat. **31**:301 (May) 1949.

The interesting observation is made that mortality among patients with lobar and bronchopneumonia at the Pediatric Clinic in Perugia since 1932 was no higher when classic procedures

were used than when sulfonamide drugs were administered. It is stressed that tried classic therapy must not be neglected when sulfonamide drugs are used for infants with pneumonia. The value of sulfonamide drugs in preventing pneumonia and in shortening the duration of the illness is not considered in establishing the statistics given. Death from bronchopneumonia is more frequently referable to the primary cause or to the nutritional state of the patient than to the pneumonitis itself.

HIGGINS, Boston.

APICAL PULMONARY NEOPLASM IN A CHILD. L. MATTEUCCI, Clin. pediat. **33**:246 (April) 1951.

A chest roentgenogram of a child of 8 years showed a large rounded shadow at the apex of the left lung. The first diagnosis was epituberculosis; but when the tuberculin reactions were found to be negative, the diagnosis was changed to pulmonary neoplasm. The tumor was removed surgically and was shown by histological examination to be an adenomyxosarcoma.

HIGGINS, Boston.

AIR-CONTAINING CYSTS OF THE LUNGS IN CHILDREN. ACETO GIACOMO, Clin. pediat. **33**:369 (June) 1951.

A roentgenogram of the chest of a 2-year-old boy with osteomyelitis of the humerus revealed the presence of several large emphysematous blebs, an unexpected and asymptomatic pathological finding.

HIGGINS, Boston.

ASPIRATION OF MILK INTO THE LUNGS AS A CAUSE OF SUDDEN DEATH IN INFANTS. C. ZUNIN, Lattante **22**:198 (April) 1951.

Two premature infants, both of whom were gaining weight satisfactorily, were found dead in bed. Necropsies indicated that the probable cause of death was aspiration of vomited milk.

HIGGINS, Boston.

SOME CHARACTERISTICS OF THE PULMONARY VESSELS IN INTRAUTERINE LIFE. E. CIFARELLI, Lattante **22**:237 (April) 1951.

Serial sections of the lungs of embryos and fetuses have been studied to explain the development of possible routes of collateral circulation in some congenital pathological conditions.

HIGGINS, Boston.

CHANGES IN THE IONS AND THE PROTEINS OF THE BLOOD OF INFANTS IN THE COURSE OF BRONCHOPNEUMONIA. C. STICCA, Minerva pediat. **1**:445 (Dec.) 1949.

Observations on 10 infants revealed that there was usually a low blood-chloride and low salt content at the onset of bronchopneumonia. In the cases in which there was marked dyspnea, the blood chloride was found to be elevated and the alkali reserve to be slightly lowered.

HIGGINS, Boston.

SIMULTANEOUS VISUALIZING OF THE ANTERIOR AND THE POSTERIOR MEDIASTINUM AFTER INSUFFLATION BY THE PERIDURAL ROUTE: 3-DIMENSIONAL STRATIGRAPHIC STUDY. G. SANSONE and A. DE MAESTRI, Minerva pediat. **3**:332 (June) 1951.

The posterior mediastinum was investigated roentgenologically after the injection of oxygen at the level of the 12th dorsal vertebra. As much as 500 cc. of oxygen could be injected in the older children. The method is described as easy and well tolerated by the patient. Roentgenograms obtained by stratigraphy give views of both the anterior and the posterior mediastinum, including the great vessels.

HIGGINS, Boston.

BRONCHOPNEUMONIA WITH A FALSELY POSITIVE WASSERMANN TEST. E. GRASSO and P. MENGHI, Minerva pediat. **3**:398 (July) 1951.

Three cases of bronchopneumonia are reported in children 4, 6, and 7 years of age. Each child had positive reactions to serological tests for syphilis (Wassermann, Kahn, Meinicke) during the illness. The reactions became negative after convalescence. All tests of the parents' sera elicited negative reactions.

HIGGINS, Boston.

LÖFFLER'S SYNDROME. A. DURIO, U. GUELI, and B. PESCHLE, Pediatria **58**:928 (Nov.) 1950.

Löffler's syndrome is characterized by pulmonary infiltration and eosinophilia. The illness is usually benign, but prolonged. The symptoms are mild and may include asthenia, cough, and slight fever. The pulmonary pathology may be found only from roentgenograms. A case of Löffler's syndrome is reported in an 8-year-old girl who had been subject to asthmatic attacks. The infiltration seen in the roentgenograms persisted for 10 months and then disappeared. Thirteen to 24% of the white blood cells were eosinophiles. No parasites were found upon examination of the feces.

The suggestion is made, in view of recent research with corticotropin (ACTH) and cortisone, that the syndrome may be due to an adrenocortical deficiency.

HIGGINS, Boston.

SPONTANEOUS PNEUMOTHORAX IN AN INFANT OF 28 DAYS. EMILIO ROVIRALTA ASTOUL and JOSE MARIA MUÑOZ PUJOL, Acta pediat. españ. **9**:482 (April) 1951.

A case of spontaneous pneumothorax in a baby of 28 days is presented. Delivery had been normal, and there was no asphyxia neonatorum. When the child was 12 days old, fever, cyanosis, dyspnea, and restlessness developed. Penicillin was administered, and the child became afebrile but had paroxysms of cyanosis. A roentgenogram showed what appeared to be "gaseous cysts." The entire lung did not collapse because of an adhesion which held part of the lung tissue adherent to the pleura. Some areas of cutaneous emphysema developed also. Treatment was with oxygen therapy; thoracentesis, with aspiration of 20 cc. and later 100 cc. of air, and penicillin to prevent new infections.

The authors discuss differential diagnosis, etiology, symptomatology, and prognosis. Roentgenograms are included showing the progress from the time there were two "gaseous cysts" until the involution of the process and complete recovery of the child. The etiological factors in children are (1) congenital anomalies, (2) infection, (3) trauma, (4) mechanical factors such as cough and occlusions, intrinsic and extrinsic, (5) hemorrhage in the newborn, (6) congenital cardiac malformations, and (7) results of disease or lesions in utero. This condition must be differentiated diagnostically from (1) cysts, especially gaseous, (2) diaphragmatic hernia, and (3) subpleural acute emphysemas.

ALLEN, Santa Fe, N. M.

SPONTANEOUS PNEUMOTHORAX IN AN INFANT. B. TARACENA DEL PINAL and S. RUIGOMEZ ITA, Acta pediat. españ. **9**:492 (April) 1951.

A case of spontaneous pneumothorax is reported in a child of 5 months. The condition was believed to have been precipitated by pneumonia followed by another infectious process, kala-azar. The pneumonic condition healed rapidly, but with the production of many subpleural vesicles of emphysema. In all 400 cc. of air was removed, but this was done gradually and at intervals of 12 to 24 hours. The roentgenogram showed complete collapse of the right lung, with marked deviation of the mediastinum with concavity to the right. This mechanism of collapse is a protective therapeutic process in cases such as this. The kala-azar and resulting anemia apparently had no direct relation to the spontaneous pneumothorax.

ALLEN, Santa Fe, N. M.

SEROFIBRINOUS PLEURAL EFFUSION IN A NONTUBERCULOUS INFANT. PEDRO OYARCE ROJAS and HUGO MONTES VALDEBENITO, Rev. chilena pediat. **20**:441 (Oct.) 1949.

The authors present the case of a 7-month-old infant who simultaneously had an acute pulmonary process and serofibrinous pleurisy. This pleural fluid was cultured seven times and

showed no growth. After two evacuating pleural taps, the first one followed by intrapleural penicillin, the fluid was reabsorbed. This case is interpreted as an instance of acute parapneumonic pleurisy which, because of early treatment, did not reach the suppurative state.

FROM THE AUTHORS' SUMMARY.

NONTUBERCULOUS EMPYEMA IN CHILDREN. MARIO GONZALEZ and EDUARDO VELASQUEZ, Rev. chilena pediat. **20**:503 (Dec.) 1949.

The authors report upon 132 patients with nontuberculous pleural empyema, seen at the Roberto del Rio Children's Hospital of Santiago, Chile, between the years 1940 and 1948. Of these patients, 65% were children under 4 years old. Pneumococci were the commonest etiologic agent, causing 50% of the infections in children under 2 years old and 66% in those over this age. Staphylococci were responsible for 26% of the infections in children under 3 years and for 10% in children from 3 to 12 years old. In infants under 12 months, 50% of the empyemas were caused by staphylococci.

Forty-six patients were treated only with sulfonamide drugs, 26 with penicillin, and 74 with both of these agents. The best results were obtained in the group in which penicillin was administered, and in this group, too, the mortality was lowest (4% as compared to 13% in those treated with sulfonamides exclusively).

There are very definite indications for surgical procedures, and when indicated they are the only effective measures. The indications are as follows: (*a*) incomplete evacuation of pus, (*b*) unfavorable course of the disease, (*c*) empyema due to an antibiotic-resistant organism, and (*d*) empyema due to tracheobronchial fistula.

The authors recommend large doses of penicillin, over 100,000 units, locally injected into the pleura, because by this means the number of chest punctures is reduced, and at the same time the risk of penicillin resistance is diminished. The authors comment on the present higher frequency of sterile empyema, 15% in their series, as compared with the presulfonamide era, in which it was quite exceptional. They also find that the frequency of empyema has diminished, and thus, between the years 1929 and 1939, it represented 0.83% of the admissions to the hospital, as compared with only 0.43% between the years 1940 and 1948.

FROM THE AUTHORS' SUMMARY.

A CASE OF SPONTANEOUS CHYLOTHORAX. PEDRO DANIEL MARTINEZ, Bol. méd. Hosp. inf., México **7**:528 (Aug.) 1950.

The author reports a case of left chylothorax in an infant 4 days old. It healed spontaneously with repeated punctures in 13 days. Comments are made on therapeutic procedures and on cases reported in the literature.

FROM THE AUTHOR'S SUMMARY.

A CASE OF ATELECTASIS OF THE LUNG CAUSED BY OBLITERATION OF THE BRONCHUS DUE TO PRESSURE OF PLEURITIC EFFUSION. J. SVEJCAR, Pediat. listy **4**:177, 1949.

A case of pleuropneumonia in a 7-year-old boy was observed at the First Children's Clinic. Atelectasis of the lung developed by pressure on the bronchus caused by the pleuritic effusion. There was a displacement of the heart shadow and of the mediastinum to the side of the effusion. After thoracic puncture and removal of 0.75 liter of exudate, return to normal position was observed. This is the only case of atelectasis of the lung due to pleuritic effusion so far described in the pediatric literature.

FROM THE AUTHOR'S SUMMARY.

## Diseases of Gastrointestinal Tract, Liver, and Peritoneum

CRITICAL STUDY OF BIOLOGIC TESTS IN DIAGNOSIS OF SPASMOPHILIA IN THE CHILD. II. P. GIRARDET and H. ZELLWEGER, Helvet. paediat. acta **6**:455 (Nov.) 1951.

In a study of hypocalcemia induced by estradiol (ovocyclin®) administration, according to the method of Klotz and Barbier, in 47 normal and spasmophilic children, the authors have obtained extremely variable results, and they conclude that this test is of no value in the diagnosis of spasmophilia in childhood.

FROM THE AUTHORS' SUMMARY.

A Clinical Case of Cystic Fibrosis of the Pancreas. C. Lombroso, Minerva pediat. **1**:461 (Dec.) 1949.

A 2-year-old girl had repeated severe respiratory infections, which responded to penicillin therapy. Intermittent attacks of diarrhea with fatty stools and the finding of a marked trypsin deficiency in the duodenal secretions led to a diagnosis of cystic fibrosis of the pancreas, claimed to be the first case reported in the Italian medical literature. The child has gained weight and shown clinical improvement; she has been receiving penicillin prophylactically, glandular extracts, and a high caloric diet, and hydrolyzed protein has been fed.

Higgins, Boston.

Clinical Characteristics of Hepatic Cirrhosis in Infancy. P. Montenovese, Minerva pediat. **1**:470 (Dec.) 1949.

Two cases of hepatic cirrhosis in infants are reported. In one an autopsy was done, and in one a biopsy of the liver is reported.

Higgins, Boston.

Four Cases of Hepatic Dwarfism with Particular Attention to the Carbohydrate Metabolism. R. Bulgarelli, Minerva pediat. **2**:109 (March) 1950.

Of four cases of hepatic dwarfism, one was diagnosed as chronic liver steatosis of the Björum type (*Acta pediat.* **6**:225, 1926), one as congenital hepatomegalic cirrhosis, and two as glycogen disease. A biopsy of the liver is necessary for an accurate diagnosis in every case of hepatic dwarfism.

Higgins, Boston.

Chloromycetin in the Gastroenteritis Syndromes of Infants. C. F. Cerruti and M. Scarzella, Minerva pediat. **2**:220 (May) 1950.

Chloramphenicol (chloromycetin®) proved very efficacious in the treatment of several types of enteritis in 13 children.

Higgins, Boston.

Symphysis of the Testis and the Appendix in a Congenital Inguinal Hernia. A. Vero Bo, Pediatria **57**:941 (Nov.) 1949.

A 4-year-old boy was operated upon for a congenital inguinal hernia. The appendix was found in the hernial sac adherent to the testis.

Higgins, Boston.

Attempts at Isolation of the Bacterium Dysenteriae from the Feces of Infants with Enteritis. L. Federico Signorini, Riv. clin. pediat. **49**:417 (June) 1951.

Sixty-five cultures were made from the stools of breast-fed infants with enteritic syndromes. Only once was Shigella isolated. The results of these findings are discussed with reference to the Italian literature on the subject.

Grulee, Evanston, Ill.

Impaled Foreign Body in the Duodenum of a 9-Month-Old Infant. E. Roviratta and J. Picanol, Acta pediat. españ. **9**:65 (Jan.) 1951.

The authors present the case of a child with an open safety pin impaled in the third portion of the duodenum. Although most foreign bodies are expelled spontaneously, open safety pins and hair pins may prove troublesome. Roentgenograms for the purpose of watching the movement of the body and conservative treatment were tried, but, when the pin stayed in the same position for three days and the temperature became elevated, surgery was deemed necessary. Methods suggested by Ferre, including use of atropine and postural changes, were tried but were not effective. Use of a sound or bougie was not tried for fear of perforation.

The pin was found to have lodged with the head and point 3.5 cm. apart, and a large area of edema was noted in the third portion of the duodenum. There was some serous drainage, and

adhesions were beginning to form between the duodenum and contiguous viscera. An incision into the duodenum was necessary to free the head of the pin. Penicillin and streptomycin were administered before and after the operative procedure, and recovery was uneventful.

ALLEN, Santa Fe, N. M.

CONGENITAL MEGACOLON: TREATMENT BY PARTIAL RECTOSIGMOIDECTOMY. ARNULFO JOHOW, GUILLERMO LLORDA, and ROSA VOLOSKY, Rev. chilena pediat. **12**:547 (Dec.) 1950.

The latest etiopathogenic concepts of congenital hypertrophic dilatation of the colon (Hirschsprung's disease) are reviewed and it is stressed that the real cause does not lie in the hypertrophic part of the colon, as was formerly believed, but in the stenosed section of rectum or sigmoid. In this narrow segment, histological studies have demonstrated, there is an absence of ganglion cells and other neurological disorders which cause the condition.

The first case of Hirschsprung's disease in Chile in which operation was done by Swenson's technique, based in the above-mentioned pathogenic concept, is described.

FROM THE AUTHORS' SUMMARY.

MALFORMATIONS OF THE ANORECTAL CANAL. CARLOS HERRERA MARTINEZ, Rev. Hosp. niño **13**:7 (July-Dec.) 1950.

The author discusses the various types of congenital abnormality of the anorectal canal and illustrates them with diagrams. Many of these malformations can be interpreted as arrest or abnormality in development at approximately the seventh or eighth week of embryonic life. The essential factor in treatment is to establish the continuity of the epithelium between the rectum and the skin and to prevent posterior constriction. All such patients must be treated in the hospital, and, when vital indications are present, treatment should be early. The patient must be closely observed and controlled for at least one year after operation.

KEITH, Rochester, Minn.

A CASE OF CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEOESOPHAGEAL FISTULA TREATED BY PRIMARY ESOPHAGEAL ANASTOMOSIS. O. NAVARRO FRANCO, Bol. méd. Hosp. inf., México **7**:14 (Feb.) 1950.

The author presents a case of congenital atresia of the esophagus with tracheoesophageal fistula, in which he performed a primary anastomosis, removal of fistula, and gastrostomy. The child has survived up to this date, and this is attributed to successful preoperative and postoperative care. Regarding this malformation the author firmly stresses the data which should be taken into consideration in order to establish a correct diagnosis.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL DIAPHRAGMATIC HERNIA. JUAN RODRIGUEZ JIMENEZ, Bol. méd. Hosp. inf., México **7**:861 (Dec.) 1950.

The author reviews 23 cases of congenital diaphragmatic hernia which have been seen in the Hospital Infantil in seven years, an incidence of 0.054%. Eighty-seven per cent of the cases were in children one year old or less. Vomiting was the main symptom (18 patients), and it began at birth (16 of 18 patients). Blood in the vomitus was seen in 11 of the 18 cases. Dyspnea and cyanosis were seen in 25% of the cases. Diaphragmatic hernia is frequently found together with other malformations (9 cases), such as intestinal occlusion, malrotation, or stenosis. The diagnoses were confirmed with the aid of roentgenograms.

The variety of congenital diaphragmatic hernia most frequently found was one through the esophageal hiatus. Sixty per cent of recoveries were obtained through surgical procedures. The most frequent postoperative complications were bronchopneumonia, pneumothorax, and hemothorax.

Preoperative and postoperative care is fundamental in order to obtain successful results.

FROM THE AUTHOR'S SUMMARY.

REVIEW OF HIRSCHSPRUNG'S DISEASE WITH A REPORT OF ONE CASE. FERNANDO MARTINS, Arq. pediat. **22**:7 (July) 1950.

A fairly complete review of the congenital megacolon syndrome is given. There is a long discussion of medicinal treatment and a very brief discussion of surgical treatment. In the bibliography, the articles that have appeared in the past few years relative to surgical management were not noted.

CHRISTOPHERSON, Wilmette, Ill.

PANCREOPATHY IN EARLY CHILDHOOD. RUDOLF GARSCHE, Med. Klin. **45**:1044 (Aug. 25) 1950.

Celiac disease, cystic fibrosis of the pancreas, and meconium ileus are discussed in an interesting manner.

AMBERG, Rochester, Minn.

PANCREATIC ENZYME STUDIES IN CHILDHOOD. H. U. SAUERBREI and K. B. STARKE, Monatsschr. kinderh. **97**:28 (May) 1949.

Determinations of trypsin, diastase, and lipase in duodenal juice were done in 90 children. While values for trypsin and diastase increased with age, lipase remained at a rather constant level in normal children. Children with dyspepsia and diarrhea had a very low diastase content which rose during recovery; trypsin and lipase values remained normal. The same findings were noted in patients with infectious enteritis. Patients with celiac disease showed low lipase values and normal trypsin and diastase values. Normal readings were seen in patients with progressive muscular dystrophy and epidemic hepatitis. Low diastase content and normal trypsin and lipase values were found in patients with glycogen-storage disease.

HARTENSTEIN, Chicago.

CELIAC DISEASE AND ITS TREATMENT WITH COMPONENTS OF THE VITAMIN B COMPLEX. JOHANNA DIEMAND-MEYER, Wien. klin. Wchnschr. **63**:590 (Aug. 17) 1951.

It is reported that 17 patients with celiac disease, some cases very severe, responded very well to treatment with vitamin B complex or some of its constituents, such as nicotinamide and riboflavin.

AMBERG, Rochester, Minn.

SURGICAL TREATMENT OF CONGENITAL MALFORMATIONS OF THE DUODENUM. R. DUBOIS and J. DALHEM, Acta pædiat. belg. **2**:1, 1948-1949.

The authors describe two cases of congenital duodenal obstruction with surgical intervention and death. The presenting symptom was vomiting of bile-colored material. The possible causes for such obstruction are true atresia, congenital obstructive external bands, or inflammatory adhesions. The need for surgery at an early date, before the child's condition has become critical, is emphasized, and it is later pointed out that a duodenojejunal anastomosis provides the best operative results, since the mere removal of bands and adhesions which seem to be the cause of the obstruction does not assure the patency of the lumen of the duodenum, as demonstrated by one of their patients who had intraduodenal obstruction in addition to external bands.

GLASER, Chicago.

GASTRIC EMPTYING TIME OF NORMAL INFANTS. H. LEDUC, Acta pædiat. belg. **3**:161, 1949. 1949.

The minimal, maximal, and most frequently observed (average) emptying time of the stomach of 50 infants was studied by roentgenography. Forty-three different substances were introduced into the stomach and the results tabulated. The author comes to the conclusion that, whereas a feeding interval of three hours for breast-fed infants is physiologically normal, it is not so for artificially fed infants, for whom the interval should be longer.

GLASER, Jerusalem, Israel.

FARBER TEST FOR DIAGNOSIS OF CONGENITAL ATRESIA OF THE GASTROINTESTINAL TRACT. VACLAV TOSOVSKY, Pediat. listy **4**:261, 1949.

A description of the Farber-test technique is given. FROM THE AUTHOR'S SUMMARY.

CONGENITAL STENOSIS OF THE DUODENUM, SUCCESSFULLY TREATED BY DUODENOJEJUNOSTOMY. J. ZELENKA, J. HNATEK, V. TOSOVSKY, and A. PISKACOVA, Pediat. listy **6**:115, 1951.

A case of congenital stenosis of the duodenum, in which operation was done on the 18th day after birth and there was the complication of severe burns, is described. Retrocolic isoperistaltic duodenojejunostomy was performed. The importance of adequate preoperative pediatric nursing is emphasized, and the principles of pediatric postoperative treatment are discussed.

FROM THE AUTHORS' SUMMARY.

CHANGES IN THE AMINO-NITROGEN CURVE IN THE BLOOD AS A DIAGNOSTIC AID IN CYSTIC FIBROSIS OF THE PANCREAS. J. SVEJCAR and M. BELSKA, Pediat. listy **6**:320, 1950.

The case is reported of a boy aged 3¼ years with fibrocystic disease of the pancreas. The clinical signs were chronic diarrhea, bronchitis, clubbed fingers, and enlarged abdomen. The diagnosis was confirmed by the amino-nitrogen curve which remained flat after gelatin administration, in contrast to the curve after the administration of protein hydrolysates. Determination of this curve after ingestion of natural cow's milk, dried milk, and buttermilk showed similar differences; the highest increase in the amino-nitrogen level occurred after ingestion of buttermilk. Treatment with a diet based on buttermilk and the administration of pancreatin was followed by rapid recovery and gain in weight. FROM THE AUTHORS' SUMMARY.

ATRESIA OF THE ESOPHAGUS: RECONSTRUCTION OF THE INTRATHORACIC ESOPHAGEAL CONTINUITY BY TRANSPLEURAL APPROACH IN 2 INSTANCES. TYGE C. GERTZ, Acta pædiat. **37**:391, 1949.

The author presents two cases of atresia of the esophagus with tracheoesophageal fistula. In both cases the esophageal continuity was reconstructed by the transpleural approach. One of the patients is now 5 months old and doing well, but the other died six days after the operation as a result of a cardiac malformation. Autopsy showed a sufficient anastomosis. The advantages of the transpleural approach are emphasized, particularly the significance of being able to put the diaphragm out of action temporarily and of thus obtaining a freer respiration, with consequently reduced risk of pulmonary complications postoperatively. Gastrostomy did not prove necessary in either of the cases reported. FROM THE AUTHOR'S SUMMARY.

INTESTINAL OBSTRUCTION IN THE NEWBORN: REPORT OF 4 CASES TREATED SURGICALLY. TYGE C. GERTZ, Acta pædiat. **37**:402, 1949.

Four cases of intestinal obstruction in infancy are presented. All the babies underwent operation, and all recovered. In one instance the obstruction was due to atresia of the ileum, in another to a stricture immediately distal to the duodenojejunal junction. Side-to-side anastomoses were constructed in both patients. The third case was one of meconium ileus, and the intestinal passage was established after injection of a solution of pancreatin into the small intestine. The fourth patient had a common ileocolic mesentery attended with volvulus of the midgut, and he recovered after detorsion of the volvulus followed by freeing of the adhesions in accordance with Ladd's method. On the basis of these four cases, the author discusses diagnosis and differential diagnosis in intestinal obstruction during infancy, emphasizing particularly the importance of roentgenologic examination. FROM THE AUTHOR'S SUMMARY.

INCIDENCE OF INFECTIOUS HEPATITIS IN STOCKHOLM AND MEASURES FOR ITS PREVENTION. O. GERTZÉN and J. STRÖM, Svenska läk.-tidning. **46**:1077 (May 20) 1949.

Of 624 cases of acute hepatitis at the Hospital for Epidemic Diseases in Stockholm, 407 were of the common epidemic type, 136 of the inoculation-hepatitis type, and 81 were classified as

undetermined types. Epidemic hepatitis is commoner in children, while inoculation hepatitis is rare in infancy and slowly increases in frequency with age. In about half the cases of epidemic hepatitis with known contact, the source of infection was a member of the family. The authors discuss the mode of transmission and emphasize the role that abortive cases and healthy carriers may play. They believe that the disease is transmitted by personal contact and by the alimentary route, and not by air-borne infection. In order to prevent the spread of infection, they recommend isolation of all manifest cases and careful examination and supervision of all persons in the patient's surroundings. Tentatively, gamma globulin may be used as prophylaxis.

WALLGREN, Stockholm, Sweden.

DUODENAL AND GASTRIC ULCER IN CHILDREN. FRITZ KARLSTRÖM, Svenska läk.-tidning. **46**:1218 (June 3) 1949.

During the last five years 30 children with peptic ulcers had been treated in Swedish hospitals. The disease is most prevalent at 10 to 15 years of age and is more frequent in boys than in girls; duodenal ulcer is more frequent than gastric ulcer. The symptomatology corresponds to that of adults. Treatment is generally successful, and indications for operation should be more restricted than in older people.

WALLGREN, Stockholm, Sweden.

EPIDEMIC DIARRHEA IN INFANTS. E. FRISELL and G. LAURELL, Svenska läk.-tidning. **46**:2481 (Nov. 18) 1949.

In two epidemics of diarrhea in 1949 at the Sachs' Children's Hospital, 31 infants became ill. Coli bacilli (Escherichia coli), type D 433, were cultivated from the stools and upper respiratory passages in 97.6% of the cases. In one infant who did not have diarrhea the same agent was recovered.

WALLGREN, Stockholm, Sweden.

AUREOMYCIN TREATMENT OF DYSPEPSIA IN INFANTS. J. H. MAGNUSSON, G. LAURELL, E. FRISELL, and B. WERNER, Svenska läk.-tidning. **46**:2533 (Nov. 25) 1949.

The successful aureomycin treatment of seven infants with diarrhea due to Escherichia (Bacterium) coli, type D 433, is reported.

WALLGREN, Stockholm, Sweden.

THERAPEUTIC EFFECT OF DIET IN ACUTE HEPATITIS. OLOF GERTZÉN, Svenska läk.-tidning. **47**:601 (March 17) 1950.

The author has treated 97 patients with acute hepatitis with protein-rich diet, 56 patients with a diet rich in carbohydrates, and 54 patients with fat-rich diet. The caloric content of these different diets was 3,000. There was no statistically significant difference in the three groups as to the duration of the necessary stay in the hospital or as to results of thymol turbidity tests, urobilin, bile acids, and bilirubin.

WALLGREN, Stockholm, Sweden.

METHIONINE TREATMENT OF ACUTE HEPATITIS. J. STRÖM, Svenska läk.-tidning. **47**:613 (March 17) 1950.

One hundred twenty-five children with mild or moderately severe acute hepatitis were treated with methionine, and the same number (every second patient) were used as controls. No statistically significant difference was found as to the course of the disease in these two groups.

WALLGREN, Stockholm, Sweden.

MESENTERIC CYSTOMA. BJÖRN LIND, Tidskr. norske lægefor. **69**:621 (Nov. 1) 1949.

A case of mesenteric cystoma in an 8-year-old girl is reported. She had always had a distended abdomen which had gradually increased without causing trouble. Two years before admission she had an attack of severe abdominal pains lasting for three to four hours. One day before admission similar pains started again. At examination the abdomen was distended, with normal findings upon palpation. A puncture yielded protein-rich serous fluid. Roentgenologic

examination revealed dislocation of the cecum and ascending colon cranially. At laparotomy a multilocular cyst was found, weighing 6,150 gm. Anatomically, it was a lymphectatic multilocular mesenteric cyst. The postoperative course was uneventful.

WALLGREN, Stockholm, Sweden.

ABDOMINAL RECTOSIGMOID RESECTION IN HIRSCHSPRUNG'S DISEASE. C. C. WINKEL SMITH, Ugesk. læger **112**:216 (Feb. 16) 1950.

Report is made upon seven children, aged 3 months to 5 years. In five of them there were normal movements of the bowel from the second day after operation. All seven children were discharged in a satisfactory state of health.

WALLGREN, Stockholm, Sweden.

CYSTIC FIBROSIS OF THE PANCREAS. J. HOWARD and L. HESSELVIK, Upsala läkaref. förh. **54**:53 (March 15) 1949.

Report is made from Sweden of seven patients with cystic fibrosis of the pancreas, with special study of the amino acid digestion and absorption after gelatin ingestion.

WALLGREN, Stockholm, Sweden.

CYSTIC FIBROSIS OF THE PANCREAS WITH THE CLINICAL PICTURE OF VIRUS PNEUMONIA. I. VAN DER HAL, Maandschr. kindergeneesk. **18**:381, 1950.

A 6-week-old infant presented the clinical and roentgenographic picture of interstitial plasmocellular pneumonia: An apparently complete recovery was followed by a fatal relapse. Autopsy revealed a congenital pancreatic fibrosis.

VAN CREVELD, Amsterdam, Netherlands.

## Nervous Diseases

INFLUENCE OF HYPOGLYCEMIA UPON THE ELECTROENCEPHALOGRAM IN IDIOPATHIC EPILEPSY. BIASSET, BUGNARD, F. A. GREZES-RUEFF, C. GREZES-RUEFF, and PLANQUER, Presse méd. **56**:778 (Nov. 6) 1948.

The authors studied the effects of intravenous administration of insulin (1 unit per 4 kg. of body weight) in idiopathic epilepsy. Whereas in normal persons the electroencephalographic tracings showed at most a feeble increase in amplitude, without slowing, tracings obtained from patients with idiopathic epilepsy showed multiplication of already-existing abnormalities, appearance of typical spike-wave patterns, or less typical abnormal rhythms.

This simple and harmless test should help to prove the diagnosis in patients who are suspected of having idiopathic epilepsy but who show few or no abnormalities in routine electroencephalograms.

DAFFINEE, Melrose, Mass.

CLINICAL PSYCHOLOGIC STUDY OF A MICROCEPHALIC. M. SCHACHTER, Ann. pædiat. **177**: (Aug.) 1951.

Medical history and results of a Rorschach test in a microcephalic child are reported. While a Binet-Simon test showed imbecility, the more differentiating Rorschach test explained why the child could acquire, within a few months, the rudiments of writing and an improvement of his behavior. His later mental development is going to be followed up according to a definite plan. The author has not been able to find whether the Rorschach test has been used before in microcephalics.

FROM THE AUTHOR'S SUMMARY.

POLYNEURITIS CEREBRALIS. M. FLURY, Helvet. pædiat. acta **6**:62 (Feb.) 1951.

A case is reported of unilateral paralysis of the facial, glossopharyngeal, and hypoglossal nerves in a girl aged 11 years. The cerebrospinal fluid was found to be normal. The history revealed merely that the child suffered prolonged exposure to cold while skating immediately prior to the occurrence of the lesion. In the absence of other causal factors a diagnosis of polyneuritis was made. Nine further cases of isolated cranial-nerve palsies of unknown origin

(with normal cerebrospinal fluid) are described and are classified by the author as cerebral polyneuritis. All patients were admitted for diagnosis to the fever wing of the Wilhelmina Hospital.

FROM THE AUTHOR'S SUMMARY.

CRITICAL REVIEW OF BIOLOGIC TESTS IN THE DIAGNOSIS OF SPASMOPHILIA. P. GIRARDET and H. Zellweger, Helvet. pædiat. acta **6**:325 (Aug.) 1951.

A study was made of the urinary excretion of calcium after intravenous injection of calcium gluconate in spasmophilic and normal children (calciuria test). This method of diagnosis is clinically of no use, especially because the difference in calcium excretion between spasmophilic and normal children is not significant.

FROM THE AUTHORS' SUMMARY.

MULTIPLE OCCURRENCE OF INFECTIOUS ASEPTIC MENINGITIS (VIRUS INFECTION? LEPTOSPIROSES?). FRITZ LASCH and EMMERICH MORITZ, Schweiz. med. Wchnschr. **79**:1237 (Dec. 24) 1949.

From April, 1948, to June, 1949, seventy-six cases of a nonbacterial meningitis were observed, with apparently a fair number in children. The greatest number were seen from May through August. A high fever lasted 4 to 27 days. The cerebrospinal-fluid pressure was elevated, and as a rule white blood cells were present, sometimes in great numbers, preponderantly polymorphonuclear leucocytes. Only in one case was a transitory paresis of the facial and hypoglossal nerve seen. It is possible to differentiate this form of meningitis from the purely meningeal form of acute anterior polymyelitis. All patients recovered without any defects. Similarities exist between this disease and the meningitis due to Leptospira which was proved in a case of a woman working regularly with pigs. Some patients' blood showed cold agglutination.

AMBERG, Rochester, Minn.

POLYNEURITIS FROM SULFONAMIDES IN CHILDREN. G. CADEDDU, Ann. ital. pediat. **2**:410 (Oct.) 1949.

The author describes five patients with polyneuritis observed after sulfamide treatment against the Meningococcus meningitis, and he notes the importance of thiamine and the metabolic disturbances due to deficiency of this vitamin in the pathogenesis of these diseases.

FROM THE AUTHOR'S SUMMARY.

HYPNOTHERAPY IN CHOREA MINOR IN CHILDREN. S. STEFANINI, Clin. pediat. **33**:23 (Jan.) 1951.

By hypnotherapy, the author refers to sedation and not to hypnotism. He used phenobarbital sodium and a belladonna preparation, and he claimed quick and complete recovery in 12 to 16 days.

HIGGINS, Boston.

ENCEPHALOGRAPHIC FINDINGS IN LITTLE'S DISEASE. C. STICCA, Lattante **22**:257 (May) 1951.

Encephalograms were obtained on 51 children with Little's disease. The ventricles were small in 2 cases and large in 30; in 6 there was marked hydrocephalus. The lateral ventricles were asymmetrical in 21 cases. The sulci appeared normal in 24 cases. The patients with Little's disease did not present a typical encephalographic picture, although many of them did have a slight degree of hydrocephalus.

HIGGINS, Boston.

PNEUMOENCEPHALOGRAPHY AND TRANSVERSE AXIAL STRATIGRAPHY IN THE CHILD. G. SANSONE, A. DE MAESTRI, P. DURAND and N. MACARINI, Minerva pediat. **3**:358 (June) 1951.

Stratigraphy permits many different views of the shape of the ventricle and the cisternae following air injections. Twenty illustrative roentgenograms are shown.

HIGGINS, Boston.

HYDROCEPHALITIS SYNDROME IN INFANTS AND NEWBORN. GUILLERMO GIL and ALEJANDRO MANTEROLA, Rev. chilena pediat. **20**:463 (Nov.) 1949.

The authors report six cases of hydrocephalus with known origin in infants and newborn babies. Two were due to cerebellar neoplasms, two to intracranial hemorrhage, one to encephalic tuberculomas, and one to a cerebral abscess. The difficulties of the etiologic diagnosis and the possibilities of treatment are reported. The syndrome of increased intracranial pressure presented in the cases mentioned is analyzed, and a summary of the general concepts of hydrocephalus is made.

FROM THE AUTHORS' SUMMARY.

ANATOMICAL AND CLINICAL STUDY OF CHOREA IN CHILDHOOD. TOMMASO PORCELLI, Rev. clin. pediat. **49**:391 (June) 1951.

The author relates the findings observed in 85 children (51 boys and 34 girls) with chorea admitted to the Children's Hospital of Milan, in a 10-year period. In 56 (65.88%) he observed rheumatic alterations (articular or cardiac or both) and in 12 of these cases such phenomena appeared after chorea was already established. The author also relates a case studied from the anatomopathological point of view, emphasizing especially the histological alterations of the encephalon.

GRULEE, Evanston, Ill.

TREATMENT OF INFLUENZAL MENINGITIS WITH SULFADIAZINE AND STREPTOMYCIN OR DIHYDROSTREPTOMYCIN. GUSTAVO GARDELLE, R. MARTIN JIMENEZ, J. LOPEZ, and J. S. SAENZ, Arch. méd. Hosp. inf., México **19**:163 (Oct.-Nov.-Dec.) 1950.

The results of treatment of 14 patients with meningitis due to Hemophilus influenzae are reported. All were infants under 2 years old.

The authors used a combination of sulfadiazine (0.25 to 0.30 gm. per kilogram of body weight, in aliquot doses every four hours) and either streptomycin or dihydrostreptomycin (50 to 70 mg. per kilogram of body weight per day, intramuscularly in four to six injections daily; and 25 to 50 mg., intrathecally, per injection, with the exception of the last patient, to whom no intrathecal injection was given).

There were three deaths in this series, two of them after less than 24 hours of treatment, giving a corrected mortality of 8.25%, the lowest obtained by the group. There were no untoward reactions to sulfadiazine, but there was meningeal irritation following repeated intrathecal injection of streptomycin. There were no alterations of the 8th cranial nerve worth mentioning.

Considering the results obtained in the last patient, and in two others not included in this series, the authors suggest that streptomycin be used intrathecally less frequently or not at all, especially for patients who are not critically ill.

FROM THE AUTHORS' SUMMARY.

## Psychology and Psychiatry

THE PROBLEM OF THE MENTALLY DEFECTIVE CHILD. PETER COHEN, California Med. **76**:34 (Jan.) 1952.

Continued effort is necessary not only to prevent mental deficiency but also to find methods of treating it. Meanwhile, physicians must have a keener appreciation of the feelings of parents about their retarded children and must interpret the implications of the problems in a way that the parents can understand. Further community effort is necessary to provide institutional and foster-home care for those who need it. Educational and training programs should be extended and developed for all those who can benefit from such programs.

The problem of mental deficiency is not that of the parents alone, nor of physicians, psychologists, social workers, or educators. It is a problem which requires the cooperation of all these groups for solution.

PRYOR, Redwood City, Calif.

BEHAVIOR DISTURBANCES IN EPILEPTIC CHILDREN. CHARLES BRADLEY, J. A. M. A. **146**:436 (June 2) 1951.

Behavior disturbances in epileptic children are of two types. First there is the organic type, manifesting five traits: (1) erratic variability in mood or behavior, (2) hypermotility, (3)

irritability, (4) short and vacillating attention span, and (5) a rather selective difficulty in mathematics as a school subject. In the author's experience this cluster of symptoms is found in one-half to two-thirds of all epileptics seen in office practice. The symptoms are similar to those seen in patients with known organic brain damage associated with some mental retardation but not necessarily with convulsions. The second type of behavior disturbance is psychological and variable, depending upon the reaction of the patient to his environment, associated with the extent of the stigma attached to his illness.

KIMBALL, Evanston, Ill.

THE PREVENTION OF NEUROSES. GEORGE M. LOTT, J. Pediat. **38**:259 (Feb.) 1951.

Parenteral influence is one of several factors in the production of childhood neuroses. Lott advises parents to avoid inducing repressions by means of excessive shame and guilt. Do not overtrain the child. Allow some aggressive behavior. Sympathize with the child to a certain extent, and, by constructive criticism, one may be able to help him control his emotions.

MACDONALD, Pittsburgh.

EMOTIONAL REACTIONS AND BEHAVIOR OF CHILDREN IN THE HOME. RUTH WINKLEY, KATHERINE JACKSON, and OTTO A. FAUST, J. Pediat. **38**:476 (April) 1951.

Most physicians know that an only child in an upper middle-class home is more apt to have behavior problems than the middle child in the home of an unskilled laborer. The authors show how to prove this statistically.

MACDONALD, Pittsburgh.

INFANT SPEECH: CONSONANTAL POSITION. ORVIS C. IRWIN, J. Speech & Hearing Disorders **16**:159 (June) 1951.

During the first two and one-half years of life the course of development of initial consonants is linear, that of the medial consonants is decelerating, and that of the final consonants is accelerating. Final consonants are infrequent in the speech patterns during the first half year of life, while initial consonants are more frequent than medials.

PALMER, Wichita, Kan.

CONGENITAL APHASIA: A CASE REPORT. GEORGE W. GENS, and M. LOIS BIBEY, J. Speech & Hearing Disorders **17**:32 (March) 1952.

Study was made of a child thought to be aphasic-like rather than severely mentally retarded, on the basis of symptoms of alexia and agraphia. The therapeutic methods used and the improvement noted are reported. When any child presents a psychometric pattern of significant discrepancy in the Binet and performance I.Q. and when there are no etiological possibilities to explain the discrepancy, such a child should be considered and treated as an aphasic child.

PALMER, Wichita, Kan.

EMOTIONAL FACTORS IN CHILDHOOD DISEASES. JAMES MARVIN BATY, New Orleans M. & S. J. **104**:297 (Feb.) 1952.

Establishment of a psychiatric team as a regular part of the attending staff at Boston Floating Hospital is described. The team consisted of a psychiatrist, a psychologist, a psychiatric social worker, and a nursery-school teacher. This set-up permits routine intellectual and emotional evaluation of children. The program proved to be of great help in stimulating interest in mental hygiene. The relationship of emotional and intellectual development to physiological function has become increasingly apparent as a result.

MCGUIGAN, Evanston, Ill.

EXCRETION OF PHENYLALANINE AND DERIVATIVES IN PHENYLPYRUVIC OLIGOPHRENIA. GEORGE A. JERVIS, Proc. Soc. Exper. Biol. & Med. **75**:83 (Oct.) 1950.

In 20 persons afflicted with phenylpyruvic oligophrenia, ranging in age from 2 to 42 years, with I.Q.'s of 5 to 47, the urinary output of phenylalanine varied from 50 to 20 mg. per gram of total nitrogen, that of phenylpyruvic acid, from 170 to 112 mg., and that of phenyllactic acid, from 91 to 40 mg. There was no correlation between I.Q. an amount of urinary phenyl com-

pounds. Study of the amount of phenyl compounds excreted in 24 hours by one patient with high- low-protein diets indicating that the output of phenyl compounds depended upon the amount of protein ingested.

HANSEN, Galveston, Texas.

OLIGOPHRENIA PHENYLPYRUVICA: II. CONSTANCY OF THE METABOLIC ERROR. ERNEST BOREK, ARTHUR BRECHER, GEORGE A. JERVIS, and HEINRICH WAELSCH, Proc. Soc. Exper. Biol. & Med. **75**:86 (Oct.) 1950.

Phenylpyruvic oligophrenia, a disease and metabolic derangement which is inherited as a recessive trait, is manifested by urinary excretion of large amounts of phenylalanine, phenyllactic acid, and phenylpyruvic acid and by an elevated phenylalanine concentration in the blood. Microbiological determinations of phenylalanine and phenyllactic acid in serum ultrafiltrates and in urine were carried out on 18 patients in a fasting state and on the spinal fluid in 9 patients. There was a characteristic blood level of phenylalanine for each patient but no correlation between serum level and mental performance. The amount of phenylalanine in the spinal fluid, which did not differ greatly among the various patients studied, varied from 6.1 to 8.2 mg. per 100 ml. The values between 19 and 38 mg. per 100 ml. of serum were greater than in control subjects, in the same order of magnitude as found in the blood. The findings of the authors suggest that, although the increased amount of phenylalanine is caused by the metabolic error, its blood level is determined by the ability of the kidney to reabsorb the amino acid.

HANSEN, Galveston, Texas.

AFFECTIVE DEVELOPMENT OF A CHILD DURING THE FIRST YEAR OF LIFE AND ITS IMPORTANCE IN PEDIATRICS. E. STERN, Ann. pædiat. **176**:389 (June) 1951.

The author tries to retrace the principal phases of the affective development of the child during the first years of his life. He discusses whether the affective state of the mother during pregnancy can have an influence on the development of the child. He emphasizes the importance of the relationship between mother and child and the child's need to be loved and to love, his need for security. A few types of mothers are described who have an unfavorable influence upon the development of the child. The phases of affective development and their relationship to the organic functions are discussed. The author emphasizes the necessity for giving the child satisfaction for his impulsive and affective needs, corresponding to the different phases of development, and the dangers of too unnecessary and too great frustration, all the time recognizing the necessity for certain refusals for the development of the ego. An effort is made to state some fundamental principles regarding the development of the child. Finally, the author tries to show the importance of all these facts for pediatrics and analyzes briefly the principal forms of developmental disturbances, namely, fixation, regression, arrested development, and psychosomatic disturbances. In conclusion he emphasizes the importance of these investigations for mental hygiene.

FROM THE AUTHOR'S SUMMARY.

SEX PROPORTIONS IN MONGOLISM. EROK HUG, Ann. pædiat. **177**:31 (July) 1951.

The higher sex incidence of mongolism in boys is due not only to social or lethal selection as has been surmised up till now. It is caused rather by a primary sex-specific proneness, which permits conclusions with regard to the genetic causation of mongolism. Initially the sex relation of the affected fetuses is about two boys to one girl. In later infancy the proportion is about four boys to three girls, because mongoloid boys die before and after birth more quickly than mongoloid girls.

FROM THE AUTHOR'S SUMMARY.

## Diseases of Genitourinary Tract

THE EFFECT OF PREOPERATIVE ROENTGEN-RAY THERAPY ON ARTERIAL HYPERTENSION IN EMBRYOMA (KIDNEY). J. EDMUND BRADLEY and MILES E. DRAKE, J. Pediat. **35**:710 (Dec.) 1949.

Ten patients with Wilms's tumor and hypertension were treated preoperatively with x-rays. In four patients the blood pressure fell five to eight days after the beginning of treatment. In

six patients there was no response. Hypertension recurred in one patient with the appearance of pulmonary metastases six months after nephrectomy. With irradiation of the metastases the blood pressure returned to normal.

MACDONALD, Pittsburgh.

ALCAPTONURIA. B. SIGG, Ann. pædiat. **175**:157 (July-Aug.) 1950.

After a general survey of the clinical picture, the pathological physiology, and the biochemistry of alkaptonuria, a case of a girl of 8 years with alkaptonuria is described. While there was a daily excretion of about 3 to 4 gm. of homogentisic acid (alkapton) the urinary tyrosin and phenylalanin was found to be considerably reduced below that in normal controls. In a patient with liver cirrhosis both these amino acids were present in much larger quantities. Sodium benzoate does not increase the homogentisic acid excretion and is eliminated as hippuric acid. Treatment with folic acid, ascorbic acid, vitamin K and liver was of no avail in this case. The alkaptonuria remained uninfluenced by these remedies. No liver damage could be demonstrated. A new test for homogentisic acid is given. The urine is made acid with acetic acid; then $CuSO_4$ dissolved in $H_2O_2$ is added, producing a dark-brown color in abnormal urine.

FROM THE AUTHOR'S SUMMARY.

CONDITIONS SIMULATING SEXUAL PRECOCITY. H. P. G. SECKEL, Ann. pædiat. **176**:361 (June) 1951.

A number of conditions are discussed which are apt to simulate precocious sexual development and which may give rise to differential diagnostic difficulties. They are as follows: (1) early normal sexual maturation, (2) isolated premature development of breasts and sexual hair, (3) isolated premature vaginal bleedings beyond the newborn period, due to trauma, foreign body, and hemorrhagic disease, and (4) a rare instance of unilateral premature development of breast tissue and labial hair due to congenital overvascularization of the trunk on that side. Therapeutic problems are discussed chiefly in terms of avoiding diagnostic errors.

FROM THE AUTHOR'S SUMMARY.

INFECTION OF THE URACHUS. L. GUBERN SALISACKS and E. FIGUERAS, Acta pediat. españ. **10**:47 (Jan.) 1952.

The authors present a case of infection of the umbilicus, in a 2-month-old boy, which healed spontaneously after a discharge of purosanguineous material but recurred again at the age of 8 months. The second bout was accompanied by fever, pain upon pressure in the hypogastric area, and painful urination. A pyelogram, injection with indigo carmine, and a roentgenogram all proved that the condition was due to a chronic inflammatory nonspecific infection of a persistent urachus. The author feels that the diagnosis could have been made much earlier and more simply had the discharging fluid been tested before the urachus became infected and enormously engorged. The simple proof that the fluid was urine should have sufficed.

The child recovered without difficulty.

ALLEN, San Francisco.

URINARY LITHIASIS IN CHILDREN. FELIPE GONZALEZ ALVAREZ and JORGE ZARAZAGA, Arch. argent. pediat. **36**:3 (July) 1951.

This is a brief review of the subject based primarily on reports in the literature. The authors state they have observed 21 cases over the past 18 years and have closely followed 14 of these, but they present very few details or statistics. A standardized approach to the thorough study of each patient is emphasized.

PANOS, Galveston, Texas.

TERATOGENESIS OF THE CONGENITAL DYSTOPIA OF THE KIDNEY. GEORG POLITZER, Wien. klin. Wchnschr. **63**:383 (May 25) 1951.

In a 14-year-old boy the urinary tract was examined roentgenologically because of typical urinary colic in the right lower quadrant. A stone was demonstrated, apparently in the ureter.

Since its size and shape made this unlikely, however, a dystopia of the kidney was diagnosed, and further examinations revealed a caudal displacement of the kidney, with abnormal orientation of the calices and a short ureter. The developmental features are discussed.

AMBERG, Rochester, Minn.

CONTRIBUTORY DATA TO THE NEPHRITIS-NEPHROSIS PROBLEM. L. BARTA, Paediat. danub. **6**:134 (Sept.) 1949.

The noncarbohydrate reducing capacity of urine is significantly higher in nephrosis than in nephritis. The phenomenon is ascribed to the increased excretion of intermediary products. Four cases are reported in which the high blood pressure was not due to some diffuse disturbance of renal circulation. Marked albuminuria without hematuria characterized the cases, in one of which there were all the characteristics of the nephrotic syndrome. According to the observations, there are cases of nephrosis with extrarenal "nephrotic involvement," and in a number of cases some common cause is probably responsible for both nephrosis and nephritis. It is unknown on what factor the form of the ensuing glomerulopathy depends.

FROM THE AUTHOR'S SUMMARY.

AN UNCOMMON CASE OF RENAL CALCIFICATION. KÁDAS LASZLÓ and VARGA FERENC, Paediat. danub. **6**:161 (Sept.) 1949.

After a discussion of the theories of stone formation in the kidney, the case of an 8-year-old girl is reported. She had had no symptoms or complaints before the day preceding her death, although both kidneys were filled with calculi to such an extent that, upon fluoroscopy without contrast material, both kidneys became well visible. Microscopic examination revealed renal changes similar to those observed following mercury bichloride poisoning. The stones were composed chiefly of lime. No changes could be detected in the parathyroid glands.

FROM THE AUTHORS' SUMMARY.

FURTHER EXPERIENCE WITH AN UNRESTRICTED DIET IN THE COURSE OF ACUTE GLOMERULONEPHRITIS IN CHILDREN. A. MORES and B. NAVRÁTIL, Pediat. listy **7**:11 (Jan.) 1952.

A control investigation was made of 62 of 76 children with acute glomerulonephritis who, from the beginning of treatment, had been permitted an ordinary hospital diet without any restrictions. Follow-up study from one to four and one-half years later showed that the course of the illness, both while in hospital and after discharge, was quite normal and that all children recovered without any residual findings in the urine. Normal convalescence was not influenced by ordinary physical activity (school attendance). In several patients complete recovery took several years. The persistence of nephritic changes in the urine for longer than a year does not always signify a transition to the chronic stage of the illness.

FROM THE AUTHORS' SUMMARY.

TREATMENT OF NEPHROSIS WITH A HIGH-PROTEIN DIET AND CASEIN HYDROLYSATE. GRETA HEDENSTRÖM, Acta pædiat. **38**:271, 1949.

A 5-year-old child suffering from nephrosis was treated continuously for seven weeks with a high-protein diet (2.2 gm. of proteins daily per kilogram of body weight) and large quantities of casein hydrolysate by mouth (2.4 gm. of aminopeptodrate [aminosol®] daily per kilogram). With this treatment the plasma protein values returned to normal and the child became clinically free of symptoms.

FROM THE AUTHOR'S SUMMARY.

PRECOCIOUS PUBERTY: CLINICAL PICTURE AND REMOTE PROGNOSIS. HANS-OLOF MOSSBERG, Acta pædiat. **40**:261 (July) 1951.

Various types of precocious puberty are discussed and a number are illustrated by cases of patients treated at Kronprinsessan Lovisa's Children's Hospital in Stockholm. These patients have been followed from 3 to 14 years after hospitalization, thus throwing light on the remote prognosis. The following cases of precocious puberty are described: a boy with adrenal hyper-

plasia (tumor?) in which there was an abnormal hormone production with a positive pregnancy reaction; a boy with a tumor of the testis; a girl with granulosa cell tumor, and a girl with constitutional precocious puberty. Finally, the mental and social problems of these children are discussed.

FROM THE AUTHOR'S SUMMARY.

DE TONI-FANCONI SYNDROME WITH CYSTINOSIS. ARNLJOT DRABLOS, Acta pædiat. **40**:438 (Sept.) 1951.

A case of Fanconi's syndrome is described in which the diagnosis depended upon a slit-lamp examination of the eyes and a biopsy of the conjunctiva. Attention is drawn to certain features which distinguish this case from cases recorded earlier.

FROM THE AUTHOR'S SUMMARY.

ELECTROENCEPHALOGRAM IN ENURESIS. SIV GUNNARSON and K. A. MELIN, Acta pædiat. **40**:496 (Nov.) 1951.

Ninety-six children with enuresis were selected for an electroencephalographic study. They were divided into two groups, those who had had a dry period for one year or more, and those who had always been wet. There is, apparently, a marked difference between the electroencephalographic findings in these two groups, with a marked preponderance of pathological records in the "never dry" group. This supports the theory of immaturity in the nervous system as the cause of enuresis in the always-wet children. Attention is drawn to the fact that two epileptics occurred among these children with enuresis.

FROM THE AUTHORS' SUMMARY.

FOLLOW-UP STUDY OF ENURESIS PATIENTS. HARALD HOVE, Ugesk. læger **111**:39 (Jan. 13) 1949.

Sixty-one patients, having a mean age of 9½ years, all with enuresis, were treated psychologically, without any drug therapy. At the time of discharge from the hospital after an average stay of 25 days, 44% were free of symptoms, and at the time of follow-up study 1 to 12 years later 77% were found to have recovered.

WALLGREN, Stockholm, Sweden.

BLADDER NECK STENOSIS IN CHILDREN. R. HEFFINCK, Maandschr. kindergeneesk. **18**:262 (Jan.) 1950.

The case histories of two very young girl infants presenting bladder neck obstruction are described, with clinical symptoms and cystoscopic findings. Different views concerning the cause and treatment are mentioned. Both children recovered, the first without operation, the other after transurethral incision.

FROM THE AUTHOR'S SUMMARY.

## Diseases of Ductless Glands; Endocrinology

THE EFFECT OF ANDROGEN ON SPERMATOGENESIS. DOROTHY JENSEN LUDWIG, Endocrinology **46**:453 (May) 1950.

From the data presented in this experiment, the conclusion is reached that low doses of testosterone propionate suppress the secretion of gonadotropins by the pituitary and thus indirectly injure the testis, resulting in loss of weight and inhibition of sperm formation. High doses, while they likewise inhibit the pituitary, result in a level of androgen which stimulates the seminiferous tubules directly. Thus testicular weight is maintained, and spermatogenesis proceeds in a normal manner even in the face of a diminished supply of gonadotropic hormones.

JACOBSEN, Buffalo.

AN IMMEDIATE RESPONSE OF THE DEMEDULLATED ADRENAL GLAND TO STRESS. MARVIN L. GORDON, Endocrinology **47**:13 (July) 1950.

The role of the pituitary and adrenal glands in the "alarm reaction" has been extensively investigated in recent years. However, the mechanism by which the corticotropic activity of the

pituitary is stimulated by various damaging agents is unknown. From the experiments here recorded it is concluded that the adrenal medulla is not essential for the activation of the pituitary gland by stressing agents.

JACOBSEN, Buffalo.

THE ABILITY OF LIVER PREPARATIONS AND VITAMIN $B_{12}$ TO MAINTAIN THYMUS WEIGHT IN THYROID-FED RATS HAVING GREATLY HYPERTROPHIED ADRENAL GLANDS. E. IRENE PENTZ, CLARE E. GRAHAM, DONALD E. RYAN, and DAVID KLEIN, Endocrinology **47**:30 (July) 1950.

Rats fed a deficient diet were given thyroid to increase the basal metabolic rate, thus resulting in a greater demand for nutritional factors not available in adequate amounts either in the diet or by intestinal synthesis. All animals which received desiccated thyroid alone showed at autopsy greatly enlarged adrenals and thymus atrophy. Those animals which received liver preparations, a concentrate of vitamin $B_{12}$, and cobione® (a saline solution of vitamin $B_{12}$) in addition to the desiccated thyroid had equally large adrenals but did not show a corresponding atrophy of the thymus. The protective effect on the thymus weight of the various preparations used is quantitative under the conditions described.

JACOBSEN, Buffalo.

PRODUCTION OF REVERSIBLE HYPERADRENOCORTINISM IN RATS BY PROLONGED ADMINISTRATION OF CORTISONE. C. A. WINTER, R. H. SILBER, and H. C. STOERK, Endocrinology **47**:60 (July) 1950.

With the use of cortisone in the treatment of rheumatoid arthritis and allied conditions, signs of hyperadrenocorticism may be expected in at least some patients treated over a long period of time. Reactions consisting of one or more of the manifestations of Cushing's syndrome (pituitary basophilism) have been observed in a small percentage of patients treated with cortisone. It was, therefore, of interest to determine in animals what signs of hyperadrenocorticism could be produced by daily administration of large doses of cortisone, and particularly whether the effects observed were reversible after cessation of treatment with the hormone.

By prolonged administration of large quantities of cortisone, several features of human hyperadrenocorticism have been reproduced in rats in the present experiments. The signs of overdosage with cortisone observed in the present experiments were of a temporary nature, and discontinuance of the use of the hormone was followed by prompt return toward a normal state.

JACOBSEN, Buffalo.

A METHOD FOR MEASURING THYROID HORMONE SECRETION IN THE RAT WITH ITS APPLICATION TO THE BIO-ASSAY OF THYROID EXTRACTS. WILLIAM F. PERRY, Endocrinology **48**:643 (June) 1951.

By measuring the rate of loss of radioactive iodine from the thyroid gland of the rat, an index of the secretion of thyroid hormone may be obtained. A simple procedure for the bioassay of thyroid preparations is proposed.

JACOBSEN, Buffalo.

DIABETES MELLITUS IN INFANTS AND CHILDREN. ALVAH L. NEWCOMB, Illinois M. J. **99**:204 (April) 1951.

Infants of diabetic mothers show many variations from normal. Gastric aspiration immediately after birth and delayed clamping of the umbilical cord appear to have favorably influenced the survival of these infants. The symptoms and signs of infantile diabetes are discussed. The principles of management of diabetes in infancy and childhood are briefly outlined.

BARBOUR, Peoria, Ill.

TREATMENT OF HYPERTHYROIDISM WITH RADIOACTIVE IODINE. GILBERT B. FORBES and ANNE M. PERLEY, J. Pediat. **38**:158 (Feb.) 1951.

Radioactive iodine successfully relieved the symptoms of hyperthyroidism in an 11-year-old girl. No toxic side-effects occurred. Radioactive iodine is not the treatment of choice in juvenile hyperthyroidism but is valuable when other methods of treatment are difficult or impractical.

MACDONALD, Pittsburgh.

SYNDROME OF OVARIAN AGENESIS (CONGENITALLY APLASTIC OVARIES); SHORT STATURE, MULTIPLE CONGENITAL ABNORMALITIES AND HIGH URINARY GONADOTROPINS IN A 2-YEAR-8-MONTH-OLD FEMALE. HENRY K. SILVER, Pediatrics **8**:368 (Sept.) 1951.

A proved case of the syndrome of ovarian agenesis, short stature, multiple congenital abnormalities, and high urinary gonadotropins in a 2-year-8-month-old girl is presented. Congenital anomalies included webbed neck, abnormalities of the feet, a moderate degree of cubitus valgus, and defects of the vertebrae. Only slight retardation of epiphyseal development was present by the fourth year of life. Because of the marked variations in the levels of urinary gonadotropins in this patient, it is suggested that more than one assay should be performed in a preadolescent girl before it is concluded that the gonadotropins are not increased.

FROM THE AUTHOR'S SUMMARY.

IS OBESITY AN ENDOCRINE PROBLEM? EDWARD H. RYNEARSON, Proc. Roy. Soc. Med. **44**:951 (Nov.) 1951.

The author forcefully reemphasizes the concept that fat results only from food and that there is no effective way to lose weight except by decreasing caloric intake. He doubts whether any of the endocrine glands are very often involved in obesity and knows of no glandular treatment which has been effective in reducing weight. Patients with myoedema lose weight with thyroid extract, but most of this weight is water. He has no criticism of the use of amphetamine (benzedrine® or dexedrine®) sulfate as a depressor of appetite except that the use distracts patients' attention from the importance of low-calorie diets. Whenever a patient really wants to lose and conscientiously follows dietary instructions, there is always a loss of weight, but because of failure to really follow a low-calorie diet, there are fewer successes than failures.

HEARD, Monterey, Calif.

ENDOCRINE DISEASES IN CHILDHOOD. A. RONALD, Indian J. Pediat. **17**:193 (Oct.) 1950.

A brief summary and the differential diagnosis of endocrine disorders in childhood are presented.

McGUIGAN, Evanston, Ill.

## Cutaneous Diseases; Allergy

ORAL CORTISONE IN INTRACTABLE BRONCHIAL ASTHMA: PRELIMINARY REPORT. EMANUEL SCHWARTZ, J. Allergy **22**:1 (Jan.) 1951.

Cortisone acetate was administered orally to three patients with prolonged bronchial asthma. One of them was a 10-year-old girl who had had severe bronchial asthma for three months previous to the use of cortisone. She was given 25 mg. four times a day for the first two days, then twice a day for four days, and then was maintained on a daily dose of 25 mg. There was dramatic relief of symptoms after the second dose, and she was able to return to school on the fourth day. Omission of a single maintenance dose would cause a return of symptoms. There were no side-effects.

HOYER, Cincinnati.

POLLEN SENSITIVITY IN 100 ASTHMATIC CHILDREN. LEWIS WEBB HILL, New England J. Med. **239**:1039 (Dec. 30) 1948.

The author suggests that too little emphasis is placed upon the role of pollen sensitivity in the production of symptoms in asthmatic children, and the frequent failure of scratch tests to reveal this sensitivity is mentioned. Of 100 asthmatic children 84 were found to react to pollen antigens, and these reactions were thought to be of clinical significance in most cases. The distribution of the reactions are given, as well as the number of positive reactions to environmental allergens. The author does not believe uncomplicated pollen allergy exists in asthmatic children.

WHEELOCK, Denver.

A Localized Outbreak of Tinea Capitis (M. Audouini) in Northern Ireland. J. Martin Beare and E. A. Cheeseman, Arch. Dis. Childhood **26**:149 (April) 1951.

An outbreak of tinea capitis in Newtownards, County Down, Ireland, between June, 1948, and August, 1949, is described. During this time, 368 children under 17 years old were affected, an incidence of about 12% in the population at the same ages. Of the 368 children, 304 were pupils in five schools. Boys were consistently more liable to infection than girls; 27.2% of the schoolboy population was infected, compared with 7.2% of the schoolgirls. There was no apparent association between age and incidence of infection. The different incidence of infection in the five different school communities suggested that the epidemic was more severe in some parts of the town than in others.

The organism responsible for the outbreak was Microsporum audouini; no other fungus was grown from 280 cultures made during the outbreak. A clinical description of the infection is given and the value of Wood's light in detecting infected children is emphasized.

Kelly, Milwaukee.

Vitamin Therapy in Pink Disease (Acrodynia). K. C. Chandhuri, Indian J. Pediat. **15**:190 (Oct.) 1948.

The cases of two patients with erythredema polyneuropathy (acrodynia) are presented in which there was marked improvement apparently due to large and prolonged doses of vitamin B complex. It is suggested that in some cases vitamin-B-complex deficiency may be an etiological factor.

McGuigan, Evanston, Ill.

Use of Collodion Pellicle in Pediatrics. L. Buscalioni and P. Nicolaj, Clin. pediat. **30**:349 (June) 1948.

Collodion pellicle has frequently been used in botanical research. The same procedure may be used in the study of the functioning of vessels of the skin of children. Photomicrographs of a patient with scleroderma are shown.

Higgins, Boston.

Pathogenesis of Epidermolysis Bullosa Dystrophia. B. Rondinini, Clin. pediat. **30**:377 (June) 1948.

The case of an 11-year-old girl with epidermolysis bullosa is reported. The findings of (1) groups of capillaries parallel to the skin surface, (2) diminished amounts of elastic and of reticular tissue upon skin biopsy, and (3) an increased excretion of porphyrin in the urine are mentioned as pertinent factors to consider in establishing the pathogenesis of the disease.

Higgins, Boston.

Lipids in Milk of Nursing Mothers of Infants with Exudative Diathesis (Eczema). L. Martoni, Clin. pediat. **32**:555 (Oct.) 1950.

Differential analyses of the fats in the milk of nine mothers nursing infants with eczema suggest that the content of the unsaturated fatty acids may play a role in the development of that condition. The linoleic acid content was definitely lowered in all but two cases, while the linolenic acid was increased above the normal amount in all but three cases. The percentage of unsaturated fatty acids was within normal limits, however, in all but two cases.

Higgins, Boston.

Mycobacteriology of the Skin of the Hospitalized Infant. Manuel Rodriguez, Jorge Rosselot, and Carmen Palomino, Rev. chilena pediat. **22**:275 (July) 1951.

The authors analyzed the significance of microbacteriologic flora of the skin and the different means of autocutaneous disinfection, noting the modifications in cases of malnutrition. They studied the microbacteriologic flora in 126 hospitalized infants, most of them suffering from malnutrition and multiple concomitant infections. This investigation was carried out on samples obtained from the scalp as well as from the skin of the abdomen. As many authors have stressed the coincidence of bacteriologic findings from the skin and from both nasal and pharyngeal

secretions, samples from these mucosae were also obtained. The study of the bacteriologic flora of 93 infants with normal skin revealed saprophytic organisms in 86 as compared with 26 in whom pathogenic ones were isolated. Only in eight cases were fungi found.

The findings were similar in samples from both the scalp and the abdominal skin, as well as in 49 samples taken one week afterward. Predominant among the saprophytic organisms were the nonhemolytic Staphylococcus albus (81.2% in the scalp and 71.2% in the abdominal skin). Among the pathogenic organisms, hemolytic Staphylococcus was identified in 21.4% of the scalp samples and Pseudomonas aeruginosa in 71.4 and 92.3% of the scalp and abdominal skin samples. The presence of concomitant infections as well as the nutritional status change these figures.

The study of the nasal and pharyngeal florae revealed a similarity to the skin flora. Of 92 infants, 90 presented saprophytic organisms and 34 pathogenic ones. Among the saprophytic, the nonhemolytic Staphylococcus was obtained in 78% and 56% respectively from the nasal and pharyngeal swabs. The hemolytic Staphylococcus was present in 75.7% and 46.2% in the nasal and pharyngeal samples. In the nasopharyngeal secretions a greater variety and a larger number of pathogenic colonies were isolated.

The number of pathogenic strains among those infants with skin infections was found to be significantly greater than those found in the infants with normal skin. In 12 infants with seborrheic dermatitis the microbiological flora of the skin was similar to those of infants with normal skins.

FROM THE AUTHORS' SUMMARY.

SCARLATINIFORM DERMATITIS PRODUCED BY ADMINISTRATION OF MESANTOIN. PEDRO DANIEL MARTINEZ and LUIS GOMEZ OROZCO, Bol. med. Hosp. inf., México **7**:884 (Dec.) 1950.

The authors report a case of scarlatiniform dermatitis with pharyngotonsillitis, cervical adenitis, and tongue desquamation caused by mesantoin® (methylphenylethyl hydantoin). The therapeutic test reproduced the pathological picture.

FROM THE AUTHORS' SUMMARY.

ANAPHYLACTIC PURPURA IN A 7-MONTH-OLD BOY. VICTOR SCOLPINI, R. GARCIA RODRIGUEZ, and JUAN C. ANGELILLO, Arch. pediat. Uruguay **19**:228 (April) 1948.

The authors present the case of a 7-month-old infant who presented symptoms of anaphylactic purpura in a sudden manner, two days after the onset of rhinitis of an infectious type. The symptoms appeared in crops, with the characteristic picture of anaphylactoid purpura, although without other allergic manifestations. The child recovered.

FROM THE AUTHORS' SUMMARY.

PENICILLIN THERAPY OF PURULENT SKIN INFECTIONS IN INFANCY. K. WEISSE, Kinderärztl. Praxis **16**:65 (March-April) 1948.

The author summarizes the data on penicillin therapy used against severest skin infections in 29 infants. Because of the shortage of penicillin, it was used only for children with severe infections (Staphylococcus) and only when a child's general condition was such that his life was in danger. Therapy with sulfonamides, blood transfusion, and ultraviolet irradiation was attempted before penicillin was used. The author felt that, although some children died, others recovered who would have died without the benefit of penicillin. If the skin necrosis was present, therapy was usually ineffective and the child died. Ten to twenty injections of 20,000 units each of penicillin in a solution of 200,000 units per 10 cc. of water were used. Fever was not found to be as good an indicator of the therapeutic effect as the child's general condition.

GLASER, Chicago.

MORBUS OSLER. H. GOLDECK and S. STILLER, Med. Klin. **45**:1617 (Dec. 22) 1950.

Morbus Osler, or hereditary hemorrhagic telangiectasia, usually manifests itself with epistaxis between the ages of 6 and 26 years. A boy representing a fifth generation is mentioned in whom epistaxis occurred at the age of 3½ years.

AMBERG, Rochester, Minn.

# News and Comment

## ANNOUNCEMENTS

**New Children's Hospital.**—Le Bonheur Children's Hospital, Memphis, opened June 15, 1952. The dedication was held at 3 p. m. in the courtyard of the hospital, after which, for three days the building was open to the public for inspection. On Monday, June 23, 1952 the hospital was opened for the reception of patients.

On June 14, 1952, from 5 until 10 p. m., the members of the Le Bonheur Club invited the members of the Memphis and Shelby County Medical Society and the members of the Ninth District Dental Society to inspect the building and familiarize themselves with the facilities.

The Medical Staff of the hospital, which is an open one, is fully organized, with the following officers:

F. Thomas Mitchell, M.D., Chief of Staff

James G. Hughes, M.D., Vice-President

C. Barton Etter, M.D., Secretary

J. Spencer Speed, M.D., Chief of Surgery

J. A. Danciger, M.D., Chief of Medicine.

The hospital is completely staffed and equipped for the entire care of private and charity patients, white and Negro, from prematurity to 14 years of age.

Freeman E. May is administrator of the hospital.

The resident staff will be furnished from the resident staff of the John Gaston Hospital until such time as the new hospital is accredited.

# Books

**Psychiatric Aspects of Juvenile Delinquency.** Monograph Series No. 1. By L. Bovet, M.D. Price, $1., 4 Swiss francs. Pp. 92. Columbia University Press, 2960 Broadway, New York 27, 1951.

This very valuable monograph is a direct result of the desire of the Economic and Social Council of the United Nations to find ways and means of formulating on an international basis an acceptable program for the study of crime and treatment of offenders and for international action in this field. A committee of experts, called together by the Secretary General, agreed that juvenile delinquency should be given priority in this study. Dr. Bovet, accordingly, was commissioned to draw up a concise but comprehensive summary of existing views on delinquency. This report of his is a synthesis of views and observations on a tour of several European countries and America, during which he consulted over 150 specialists of all kinds on juvenile delinquency and visited 60 institutes of diverse natures. Pediatricians interested in this field, or, for that matter, any pediatrician interested in psychological problems in children, would find the monograph extremely interesting and instructive reading.

The author calls attention to the fact that "delinquency is not the name of an illness, nor is there one simple specific psychological category for all delinquents, and for them alone. . . . The legal definition of juvenile delinquency varies from one country to another. . . . While according to the lawyer and, to a certain extent, to the sociologist and the teacher, juvenile delinquents form a well-defined group, according to the psychologist and psychiatrist delinquency is but one of the many aspects of that elusive concept, social maladjustment."

The reviewer would call the pediatrician's attention particularly to Chapter 2, on the etiology of juvenile delinquency, and to Chapter 3, on the prevention of juvenile delinquency. In the former the author gives an epitomized abstract of the psychological aspects of normal child development, with special reference to the studies of Anna Freud and Piaget.

To avoid the probability of delinquency, a child must be reared in an atmosphere psychologically conducive to the achievement of a satisfactory degree of social adaptation. He must

develop the intellectual and emotional capacity for interpersonal relationships of an unselfish nature. To achieve this, "he must experience in his immediate circle a deep, unfaltering, disinterested love, particularly from his mother or mother-substitute."

In the section "Disturbances in the Psychological Development of the Personality," the author calls attention to the fact that some children have a normal personality structure, "built according to everyday laws of psychology, but the material used for [the child's] super-ego was borrowed from antisocial personalities, and hence renders him liable to antisocial behavior and in certain circumstances to delinquency." These are children of antisocial parents. He also points out the serious consequences in the development of a child's personality which may follow any disturbance in the normal child-mother relationship, the quality of this relationship being a determining factor in the later development of personality. This has been especially emphasized by Rene Spitz in studies of infants brought up in institutions, and by Bowlby, who concluded that an emotional disturbance in early infancy is one of the most specific factors in the causation of juvenile delinquency.

The evidence submitted shows that a large percentage of adults and children appearing before the courts are neither physically nor psychologically seriously ill. They have had to face life situations sufficiently adverse to surmount their own personal "threshold" of social adaptation. On the other hand, there is a small but important number of delinquents who are constitutionally psychopathic.

The author rates as of secondary importance the possible role of housing, of crowding, or of poor neighborhoods. On the influence of the movies, radio, and press, he notes, "In the light of present knowledge, it cannot be affirmed that these amusements have any specific or major harmful influence on juvenile morality, or on delinquency in particular." Alcoholism among juveniles is of minor importance as contrasted with alcoholism in the adult members in the juvenile's family circle. In seeking a common denominator for the three facets of juvenile delinquency, biological, psychological, and sociological, the author believes that this psychological common denominator can be found in the feeling of insecurity to which any criminal tendency, from whatever source, gives rise.

Careful perusal of the chapter on prevention of juvenile delinquency emphasizes indirectly the importance of the pediatrician in any comprehensive program. Any such program would consist primarily and predominantly of a vast mental health campaign. Since the author and many other writers have shown that the psychological bases of delinquency are laid down in early infancy and childhood, the role of pediatricians would be of great importance in such a preventive campaign. Steps along this line, which have already been taken by some pediatricians, include, among others, a return to rooming in; humanizing of our pediatric wards; minimizing of the shock of separation by allowing daily visiting; the rapidly increasing change from rigid formulae and schedules to something approaching self-demand, emphasis on love, security, and indulgence in the first few months of baby's life with only gradual introduction of consistent discipline, and discussions with small parent groups, such as parent-teacher associations, neighborhood groups, and classes in adult education. "Child guidance is an indispensable weapon in the up-to-date equipment of any community which hopes to wage war successfully against juvenile delinquency and against all forms of social maladjustment."

**Parenteralflüssigkeitstherapie im Kindesalter**. By Emil Polacek. Price, 20 Swiss francs. Pp. 166, with numerous illustrations and charts. S. Karger, Holbeinstrasse 22, Basel, Switzerland, 1952.

This volume is an exhaustive review of all aspects of parenteral fluid administration in childhood. The work is based on extensive personal studies of the author and on a vast amount of world literature.

Due credit is given to the basic contributions of Gamble, Darrow, and Butler, and many of the well-known diagrams of Gamble are included in the text.

The first section of the book deals with the physiology of body fluids: distribution of fluids, water metabolism, water requirements, osmotic concentration, function of body fluids, extracellular fluid, kidney function, role of the hypophysis, and metabolism of the electrolytes.

The second section deals with the pathology and therapy: acidosis, alkalosis, dehydration due to diarrhea, lack of water intake, and vomiting or profuse perspiration. There are also

chapters on diabetes, renal disturbances, edema, and shock. In the final section the author discusses the management of the parenteral fluid: type of solutions, technique, and indications.

According to the author, parenteral nutrition is indicated in the following conditions: (1) when the child is unable to take fluid by mouth (obstruction of the digestive tract, persistent severe vomiting); (2) when peroral feeding is contraindicated (severe gastrointestinal infections, peritonitis, peptic ulcer, colitis ulcerosa, intestinal resection); (3) when there is a severe degree of undernutrition (before operating procedures, in hunger edema, severe burns).

Polacek's book provides a comprehensive account of the present status of parenteral fluid administration in children. Documented with 467 references, it also constitutes an excellent reference text.

**An Introduction to Universal Serologic Reaction in Health and Disease.** By Reuben L. Kahn, D.Sc. Price, $3.50. Pp. 155, with 112 charts and an index. Commonwealth Fund, 41 E. 57th St., New York 22, 1951.

Dr. Kahn's interest in the universal serologic reaction really began about thirty years ago, when he observed, in studying sera from syphilitic patients, varying patterns of precipitation obtained (1) by using different concentrations of sodium chloride and (2) by incubating tests at temperatures colder than 37 C. Subsequently, certain other patterns of precipitation were noted in nonsyphilitic (false-positive) sera. Through the years this investigator has studied hundreds of syphilitic and nonsyphilitic sera from man and animals. This volume represents a comprehensive report of universal serologic reactions observed in (1) normal human beings, (2) animals, such as rabbits, mice, guinea pigs, cows, and dogs, (3) syphilitic human beings, and (4) patients with yaws, leprosy, malaria, tuberculosis, and defective development. Dr. Kahn's thesis is that certain lipid substances are normally bound in tissue and are liberated during ordinary wear and tear; these substances act as antigens, probably stimulating production of reactive antibodies, which may be measured in vitro. The book contains many graphs illustrating various patterns of the universal serologic reaction, together with brief case records and pertinent discussions. The author gives a brief history of the development of the technique and discusses the significance of the universal serologic reaction in various conditions. Dr. Kahn does not propose the technique for "routine employment in medical laboratories at this time," but hopes "to open the door to studies of its value and limitations as a serologic indicator in various situations in health and in different diseases."

The index, which includes subjects and investigations, is adequate. Although the nature of the illustrative material may have regulated the shape of the page to some extent, it would have been nice to have the volume more nearly standard in size and shape.

**Nutrition and Chemical Growth in Childhood.** Vol. III. By Icie G. Macy, Ph.D., Sc.D. Price, $2. Pp. 711, with 732 tables. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.

Pediatricians, nutritionists, and others interested in human growth and development who have been using the first two volumes of this valuable work since 1942 will eagerly welcome Volume III. Those who are familiar with this unique study, from the Research Laboratory of the Children's Fund of Michigan, are well aware that the first two volumes are a treasure house of metabolic information. Eleven carefully selected normal children from 4 to 10 years of age, living under ideal conditions for accurate balance studies of energy, fat, nitrogen, and a number of minerals and other foodstuffs, were observed for a 95-day period. Four years later 11 subjects from 55 to 104 months of age were observed for 225 days, and, again, four years later 7 of the same subjects, 6 boys 103 to 146 months of age, and 1 girl 110 months of age returned for 55 days of additional study.

Volume I, concerned with evaluation, described in detail the children selected as the subjects, as well as the objectives, the methods, and the interpretation, whereas Volume II presented the original data grouped according to the children studied. The present volume, Volume III, consists largely of highly usable tabulations of calculated data, in which the information is grouped according to topics such as proximate composition and energy value of diets, carbohydrate intake and fecal excretion, fat intake, fecal excretion and absorption, and balance data for nitrogen, phosphorus, chlorine, sulfur, negative minerals (calcium, magnesium, sodium, and potassium)

and positive minerals. Under each topic the calculated data are given for each individual subject, both successively and in cumulative form, followed by tables of averages. There is a useful index for all three volumes.

Although the reviewer has not had the opportunity to check the calculations, one can be sure that the meticulous methods employed by Dr. Macy and her associates can be relied on to make these calculations of the highest value. The format of the book makes for clarity and quick reference.

These three volumes are an indispensable part of any complete nutrition library and should be available for reference for pediatricians as a source of information about human growth and development.

**Diseases of the Tropics.** By G. C. Shattuck. Price, $10. Pp. 783, with 157 tables and figures. Appleton-Century-Crofts, Inc., 35 W. 32d St., New York 1, 1951.

As a concept the term "tropical diseases" has various connotations, depending upon the reader's experience and interest. For some it means the diseases which are the leading causes of death in the tropics; for others, diseases peculiar to the tropics, and for still others, parasitological and protozoal diseases of all types. The author of this book takes a rather eclectic view, in that he includes most of the parasitic and protozoal diseases, as well as others, such as shigellosis and nutritional deficiences, which, while occurring generally over the earth's surface, have a relatively high incidence in tropical areas. One wonders immediately whether the higher incidence is a reflection of tropical climate or of lowered socioeconomic status, with consequent lower standard of living and personal and community hygiene. "Summer diarrhea," for example, probably includes a good deal of shigellosis, discussed extensively in this book; yet the disease occurs at a higher rate in the relatively poor province of Lapland, above the Arctic Circle, than in the more southerly, but technically more developed, areas of Finland.

On the other hand, tuberculosis, frequently one of the leading causes of death in the tropics, is not even included in the index of the present volume. In other respects the book appears to give fairly complete coverage and is well illustrated. As befits its historical and international importance, malaria gets a lion's share of the text and is thoroughly discussed. An interesting chapter is devoted to snakes and poisonous animals common to the tropics.

It is relatively easy to pick faults where coverage sets out to be so extensive. The chapter on shigellosis, for example, gives insufficient attention to the problem of salmonellosis and other causes of severe diarrhea, which probably deserve proportionately greater elaboration. The outline of laboratory methods for diagnosis is quite inadequate, and no mention is made of S S agar, generally recognized as the superior medium. In the treatment of this disease, furthermore, handling of the metabolic disturbance receives only brief consideration, and the important role of potassium in recovery is not mentioned.

The book will be a useful addition to the reference library of those practicing in areas of high prevalence of parasitic and protozoal diseases, but will be of only limited usefulness to pediatricians in continental United States.

**Serum Sickness.** By C. F. von Pirquet, M.D., and Bela Schick, M.D. (Translated by Schick). Price, $3.50. Pp. 130, with 33 charts. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1951.

This excellent monograph is a translation by Dr. Bela Schick of "Die Serumkrankheit," the classic by von Pirquet and Schick published in 1905. The translation is an excellent one and is particularly valuable because of the unusual circumstance that the translator is one of the original authors. This monograph is striking testimony to the value of clear and careful clinical observation. Although there is some laboratory testing of precipitins, the major conclusions are based on the simple but painstaking analysis of cases of serum sickness observed after the introduction of diphtheria and scarlet fever antitoxins.

Von Pirquet and Schick's new thesis was that the serum sickness was due to the antigen-antibody reaction and could be modified if previous injections of serum had been given. This work is a cornerstone in the building of the edifice of allergy and is as timely today as it was in 1905. Many of the later developments in the field are forecast in the section on the theory underlying the mechanism of serum sickness. All in all, this is a most valuable and enjoyable little book.

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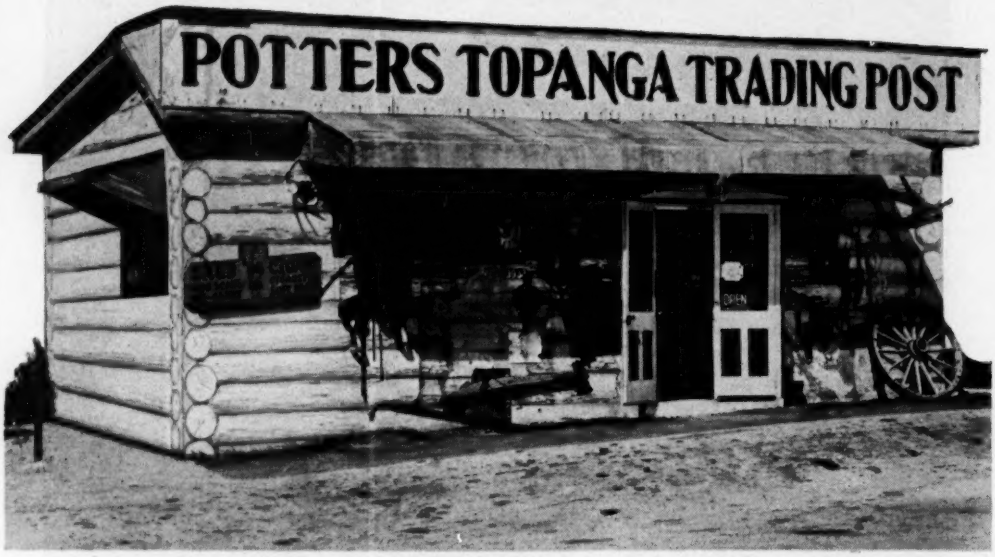


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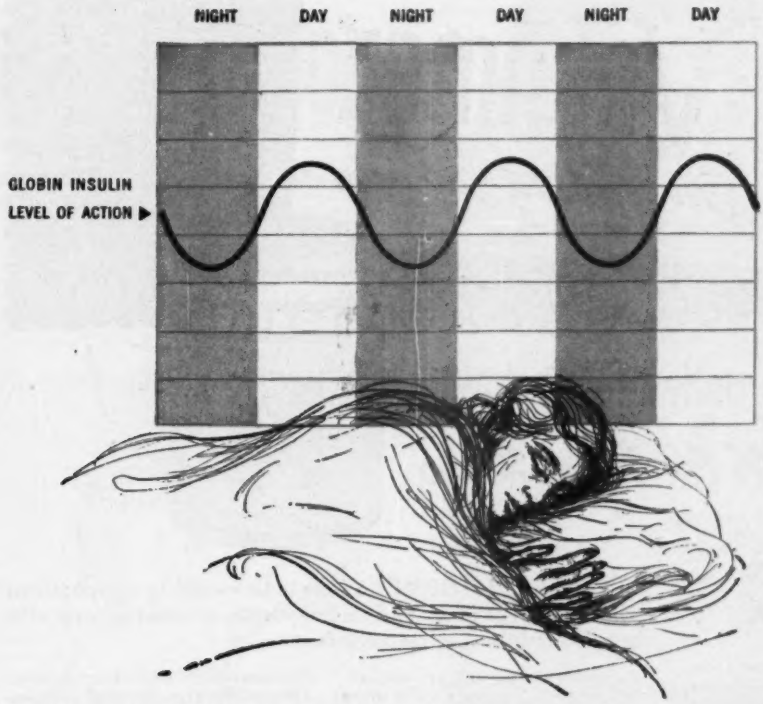


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**Proteins**—When diluted with an equal volume of water, Varamel contains 2.5 percent protein. This provides the infant daily with 3.5 to 4 grams of protein per kilogram of body weight when fed in normal amounts.

**Vitamins**—Varamel provides adequate amounts of Vitamins A, D, thiamin, niacin and riboflavin. Vitamin C must be supplied by orange juice or ascorbic acid.

**Minerals**—Varamel contains all of the mineral salts of cows milk, together with added iron, so that the infant is supplied with adequate amounts of calcium, phosphorus, iron and other minerals.

**Varamel is indicated wherever evaporated or whole milk formulas are ordinarily used . . . *Write for samples and complete details.***

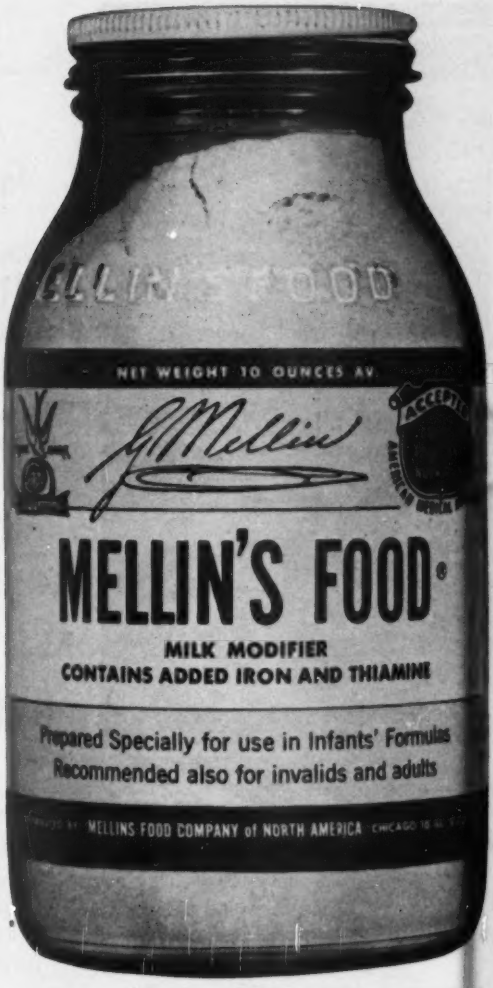
**Available only in drugstores**

**THE BAKER LABORATORIES, INC.**
**Cleveland 3, Ohio**
***Plant:* East Troy, Wisconsin. *Division offices:***
**Atlanta, Dallas, Denver, Greensboro, N. C., Los Angeles, San Francisco, Seattle**

VARAMEL

# MELLIN'S FOOD®

**MILK MODIFIER**
**CONTAINS ADDED IRON AND THIAMINE**


NET WEIGHT 10 OUNCES AV.
ACCEPTED
AMERICAN MEDICAL ASSOCIATION
MELLIN'S FOOD®
MILK MODIFIER
CONTAINS ADDED IRON AND THIAMINE
Prepared Specially for use in Infants' Formulas
Recommended also for invalids and adults
MELLINS FOOD COMPANY of NORTH AMERICA

## Prepared Specially For Use In Infant's Formulas

Mellin's Food is a dried extract produced from an infusion of wheat flour, malted barley and wheat bran, admixed with potassium bicarbonate and with added thiamine and ferrous gluconate. It contains:

| | | | |
|---|---|---|---|
| Available Carbohydrates | 79.6% | Fat | 0.2% |
| Maltose | 58.9% | Crude Fibre | 0.2% |
| Dextrins (by difference) | 20.7% | Ash | 3.9% |
| Protein—N x 6.25 | 10.3% | Thiamine | 1 mgm. per 100 grams |
| Moisture | 5.6% | Iron | 17.5 mgm. per 100 grams |

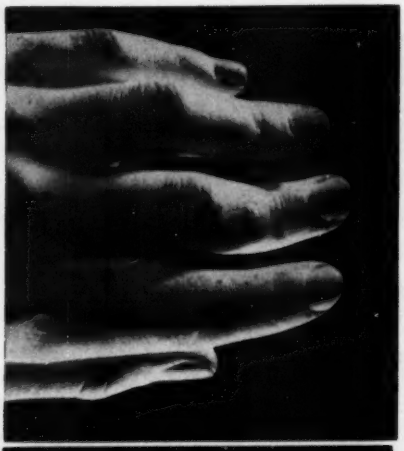
Calories 4 per gram, 115 per ounce, 25 per level tablespoonful.

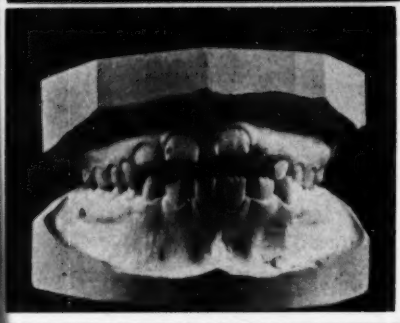
6 level tablespoonfuls supply 1.5 times the minimum daily requirement for an infant of thiamine, and 6 mgm. of iron. RECOMMENDED ALSO FOR INVALIDS AND ADULTS.

**DISTRIBUTED BY**

**MELLIN'S FOOD COMPANY of NORTH AMERICA**
**CHICAGO 10, ILL., U. S. A.**

ACCEPTED
COUNCIL ON FOODS AND NUTRITION
AMERICAN MEDICAL ASSOCIATION





# Untoward Results

## OF PERSISTENT FINGER-SUCKING

### MODEL

is 7½ years old. Unretouched photographs and description from a leading children's dental clinic.

**Hand**—sucked two middle fingers left hand since age 4. Note deformity caused.

**Mouth**—case shows deformed shape of mouth and displacement of teeth due to pressure of fingers.

*WHEN TREATMENT IS INDICATED . . .*

*--prescribe--* THUM TRADE MARK

Contains capsicum 2.34% in a base of acetone nail polish and isopropyl alcohol

***WRITE FOR FREE SAMPLE***

**NUM SPECIALTY CO.** 4614 Fifth Ave. Pittsburgh 13, Pa.

## For CONSTIPATED BABIES

ACCEPTED COUNCIL ON FOODS AND NUTRITION AMERICAN MEDICAL ASSOCIATION

A gentle laxative modifier of milk. One or two tablespoonfuls in day's formula — or in water for breast fed babies — produce marked change in stool. Send for samples.

BORCHERDT MALT EXTRACT CO.
217 N. Wolcott Ave. Chicago 12, Ill.

Borcherdt **MALT SOUP** *Extract*

SEND FOR TRIAL SAMPLE

BORCHERDT MALT EXTRACT CO.
217 N. Wolcott Ave., Chicago 12, Ill.
Gentlemen: Send me a large trial sample bottle of the Malt Soup Extracts which I have checked below.

☐ Liquid Malt Soup Extract. ☐ Dri-Malt Soup Extract.

Name.....

Address.....

City.....State.....

## *Child Health*

**Bad Habits in Good Babies.** Herman M. Jahr. 16 pages. 15 cents.

**What Does Your Baby Put in His Mouth?** Chevalier Jackson and Chevalier L. Jackson. Tells how to prevent accidents from choking and what to do if they happen. 24 pages. 15 cents.

**Keeping Your Baby Well.** 22 pages. 15 cents.

**The Case of the Crying Baby.** Herman M. Jahr. 4 pages. 15 cents.

**What to Do About Thumb Sucking.** William I. Fishbein. 6 pages. 15 cents.

**Lefthandedness.** Paul Popenoe. 8 pages. 15 cents.

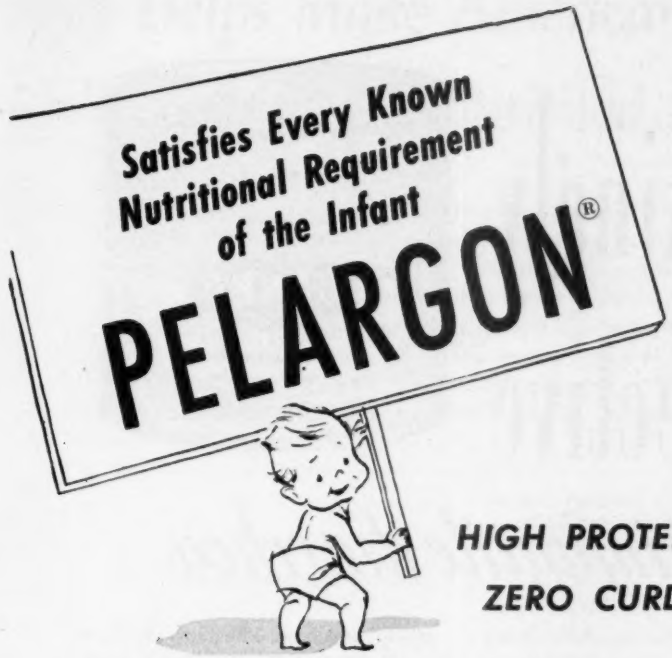
**Adoption.** W. Allison Davis and Theo Carlson. An understanding discussion of the best ways to adopt children and rear them. 12 pages. 15 cents.

**Protecting Your Child from Allergy.** William Gayle Roberts. 8 pages. 15 cents.

**The Facts About Sex.** Audrey McKeever. 16 pages. 15 cents.

Please remit with order

AMERICAN MEDICAL ASSOCIATION
535 N. Dearborn St. • Chicago 10




## HIGH PROTEIN CONTENT
## ZERO CURD TENSION

When Pelargon feedings are prescribed, mothers have the assurance that their babies are receiving a formula supplying all known nutritional essentials in adequate amounts and in a form virtually as well tolerated as human milk.

High in protein, iron, calcium and other essential minerals and vitamins, Pelargon is a readily assimilated infant food that satisfies every known nutritional requirement of the infant.

### *Plus All the Advantages of a Lactic Acid Milk*

The lactic acid of Pelargon shortens the time required to develop optimal gastric acidity, thus enhancing gastric digestion. Pelargon yields fluid casein curds of zero tension. These important digestive advantages particularly qualify it for both the regular feeding of normal babies and the special feeding of prematures, marasmic infants, and infants with digestive disorders. Pelargon is virtually as well tolerated as human milk.

**Pelargon . . . Normal Dilution**

(2 tablespoonfuls of Pelargon to 3 fluid ounces of water)

| | Per Cent |
|---|---|
| Milk Protein | 2.7 |
| Milk Fat | 2.8 |
| Carbohydrates (lactose, sucrose, starch, dextrins, maltose, and dextrose) | 7.2 |
| Lactic Acid | 0.4 |
| Minerals | 0.6 |

●

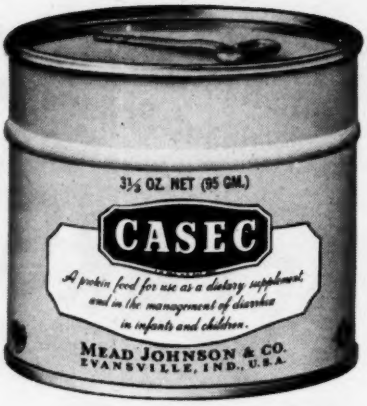
*A normal dilution of Pelargon prepared with a quart of water supplies one-third more than the generally accepted requirements of infants for vitamins A, $B_1$, $B_2$, C, and D, and for iron.*

### *Complete in Vitamins and Minerals*

Pelargon is a spray-dried lactic acid milk modified with sucrose, starch, dextrins, maltose, and dextrose, and fortified with vitamins A and D, thiamine, ascorbic acid and iron citrate. Because it is so well proportioned in all nutritional essentials and so easily digestible, Pelargon is a valuable dietary adjunct for children and adults.

**THE NESTLÉ COMPANY, INC.,** White Plains, New York

# Strikingly effective


3½ OZ. NET (95 GM.)
CASEC
A protein food for use as a dietary supplement, and in the management of diarrhea in infants and children.
MEAD JOHNSON & CO.
EVANSVILLE, IND., U.S.A.

## ...in infantile diarrhea

For three decades Casec has been strikingly effective in the symptomatic management of infantile diarrhea.

Casec (calcium caseinate) is 88 per cent protein, and provides generous amounts of calcium. When Casec is added to the formula in simple diarrhea, the physician can expect *prompt* relief from loose and frequent stools in the great majority of cases. At the same time, protein depletion is effectively prevented. The happy result is *quick relief of diarrhea* and a *rapid convalescence.*

Casec is simple to use. The mother merely adds the prescribed amount of Casec to the formula. Most physicians recommend the addition of 4 tablespoons of Casec to the formula, decreasing the amount gradually as the diarrhea clears.

Available in 3⅓ and 30 ounce cans.

MEAD'S

**MEAD JOHNSON & CO.**
**EVANSVILLE 21, IND., U. S. A.**

# Meat Helps Make Americans the World's Best Nourished People

Recent estimates of the U. S. Department of Agriculture show that the per capita consumption of meat in the United States approaches seven ounces per day. How effectively this average amount of meat in the daily diet contributes to making Americans the world's best nourished people is indicated by the following data. The figures give the average amounts of protein, iron, phosphorus, niacin, riboflavin, and thiamine provided by six-ounce servings of cooked meat (averages of the amounts furnished by six ounces each of cooked beef, lamb, pork, and veal)* and their percentages of the daily dietary allowances recommended by the National Research Council for a sedentary man (154 lb.).

| | Amounts per 6 oz.† of Average Cooked Meat | Percentages of Recommended Daily Dietary Allowances |
|---|---|---|
| Protein (Biologically complete) | 44 Gm. | 63% |
| Iron | 5.6 mg. | 47% |
| Phosphorus | 414 mg. | 28% |
| Niacin | 9.5 mg. | 79% |
| Riboflavin | 0.44 mg. | 24% |
| Thiamine | 0.50 mg. | 42% |

† 7 oz. of fresh meat, when cooked, weigh approximately 6 oz.

The important nutrients of meat, however, are not limited to those given above, for which the amounts needed for adequate nutrition have been established. Other nutrients provided by meat, but for which daily needs have not yet been established, include other members of the B complex—biotin, choline, folic acid, inositol, pantothenic acid, pyridoxine, and vitamin $B_{12}$—and many minerals essential in nutrition.

Every cut and kind of meat supplies these many nutrients for promoting health and efficiency in adults, and for health and good growth and development in children. Besides, meat is rapidly and almost completely digested, and its extractives stimulate the flow of gastric juice. Hence there is sound justification—nutritional, physiologic, and psychologic—for meat being a favorite food in the diet of the American people and in special diets prescribed by the physician.

---

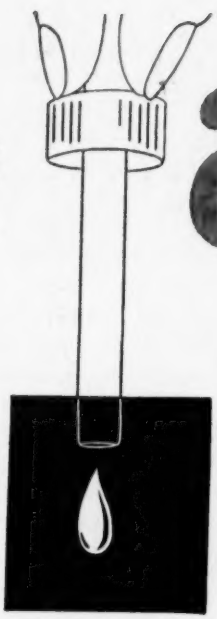
*Watt, B.K., and Merrill, A.L.: Composition of Foods—Raw, Processed, Prepared, Agriculture Handbook No. 8, United States Department of Agriculture, Bureau of Human Nutrition and Home Economics, 1950.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.

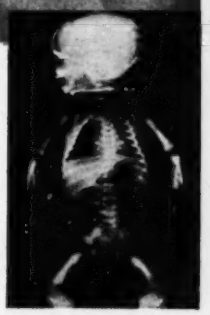
American Meat Institute
Main Office, Chicago...Members Throughout the United States

*Dispersible*
**DRISDOL®**
**WITH**
**VITAMIN A**

COMPLETELY
*Milk*
*Diffusible*



a+d



Drisdol with Vitamin A administered in milk becomes an integral part of the child's diet. It diffuses completely in milk, orange juice and other liquids without an oily film, does not separate, float or tend to adhere to nursing bottle or nipple. May also be given on the tongue or in solid foods.

Drisdol with Vitamin A contains per gram 50,000 units of vitamin A and 10,000 units of crystalline vitamin $D_2$ (calciferol). Each drop delivers 1250 vitamin A units and 250 vitamin D units.

**Dosage** for infants, 2 drops; for older children and adults, from 4 to 6 drops daily in milk.

Supplied in bottles of 10 cc. and 50 cc. with dropper.

Also Drisdol in Propylene Glycol (10,000 units of vitamin $D_2$ per gram) in bottles of 5 cc., 10 cc. and 50 cc.

*To help build a sound structure and promote growth*

Drisdol, trademark reg. U. S. & Canada,
brand of crystalline vitamin $D_2$ (calciferol)

*Winthrop-Stearns* INC.
NEW YORK, N. Y. WINDSOR, ONT.